Original Research Article

Vitamin E levels in patients with controlled and uncontrolled type 2 diabetes mellitus

Manouchehr Iranparvar Alamdari1, Shahram Habibzadeh2, Bita Shabhazzadegan3*, Mohammad Mazani4, Amir Bigdeli5, Ali Shahbazi6

1Department of Internal Medicine and Endocrinology, 2Associate Professor, Department of Infection Disease, 3PhD of Health Education and Health promotion, Social Determinants of Health (SDH) Research Center, 4Department of Biochemistry, 5Department of Internal Medicine, 6Department of General Medicine, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

Received: 03 January 2018
Revised: 05 February 2018
Accepted: 06 February 2018

*Correspondence:
Dr. Bita Shabhazzadegan,
E-mail: bitashahbaz2004@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Diabetes type 2 associates with increased oxidative stress and reduced antioxidant. Vitamin E supplementation reduces oxidative stress in diabetic patients. We intended to measure the level of this vitamin in these patients to assess its relationship in control of patients' diabetes by designing present study.

Methods: This is a descriptive and cross-sectional study and carried out on 186 patients with diabetes type 2 diagnosis. The levels of HbA1C (measured by HPLC method), TG, cholesterol, HDL, LDL and Cr were measured, and given to that the level of HbA1C lower than 7 (controlled group) and or more than 7 (uncontrolled group), patients were divided in two groups. Were designed a check list involved questions such as age and information of each patient associated with measured vitamin E level were entered into the check list and after that were analyzed data.

Results: In the existing study 186 diabetic patients were examined. From within examined patients, 129 (69.3%) were women and the rest were men and average patients age were 53.33±11.2. In this study was observed there was no direct correlation between the level of cholesterol (p=0.284), LDL (p=0.538) and HDL (p=0.362) with controlled DM II in patients while in uncontrolled diabetic the triglyceride levels was more than those with controlled blood sugar significantly (p=0.046). The average vitamin E level in patients was 1488.6±692.2 nmol/l its lowest level 114.4 nmol/l and the highest level was 6235 nmol/l.

Conclusions: The results of this study show that the vitamin E levels no significant difference between control and non-control diabetic patients.

Keywords: Vitamin E, Diabetes mellitus type 2, Antioxidant

INTRODUCTION

Diabetes is an epidemic disease round the world. Diabetes frequency of occurrence is rising in most of the populations especially in developing countries. At the moment there are 7.5 million diabetic patients in Iran. The global epidemic of diabetes mellitus has severely increased in last 2 decades and also it has been escalated from 30 million in 1985 to 285 million in 2010. If the condition keeps going like this, in 2030 there will 438 million diabetic patients according to diabetes international federation’s anticipations. Although the prevalence of both diabetes type 1 and type 2 is increasing all around the world. But the type 2 diabetes is spreading much faster than the type 1. The reasons for this phenomenon probably are the rising obesity,
decreased physical activities (which is due to the industrialization) and rising age of communities. In 2010 almost 1.6 million people (over 20) were diabetic who have been diagnosed recently. The risk of diabetes mellitus rises as age increases. In 2010, the prevalence of diabetes mellitus in United States was estimated 0.2% in less than 20 years and 11.3% in over 20 years old. In the people over 65 diabetes mellitus’ prevalence was 26.9%. The prevalence of this disease is almost as same as in all age ranges in men and women (11.8% in men over 20 and 10.8% in women over 20) global estimations predict that in 2030, the most of the diabetics will be in range of 45 to 64 years.7 The studies of the control of diabetes and its side effects have indicated that the diabetes side effect can be delayed or reduced with the control of the severe glycaemic.7 In the last decade there have been some considerations over oxidative stress and its role in causing side effects in diabetic patients. Lots of studies have indicated the high levels of oxidative stress markers.8 The increase in levels of insulin, free fatty acids and glucose can cause an increase in ROS and oxidative stress and also it can activate the stress sensitive pathway.7 In last years it has been known that the most important factor in producing free radicals in diabetes is hyper glycaemia, which increases the production of superoxide radical in mitochondria.8 It has been reported that the levels of alpha tocopherol in type 2 diabetic patient’s plasma is lower than the healthy people.9 The alpha tocopherol prescription can cause a delay in chronic side effects of diabetes.10 Also alpha tocopherol has beneficial effects on metabolically control in diabetes by its anti-oxidation effects on lipid oxidation, protein glycosylation and its sensitivity to insulin.11 The results of a 4 year old cohort study showed that for each 1 micromol/l decrease in alpha tocopherol plasma levels, the risk of diabetes rises about 22%.12 Also other study showed that consuming vitamin e in diabetic patients can significantly decrease levels of micro albuminuria and thromboxane A2 in patients with micro albuminuria.13 Other study was about effects of vitamins E and C on fat profile in patients with diabetes mellitus. The results of this study showed that consumption of vitamins E and C can significantly decrease hypertension and cause remission in insulin activity and fat profile.14 Studies showed that vitamin E has an important effect on decreasing blood pressure and blood glucose in type 2 diabetic patients.15 Of course other studies say that vitamin E cannot ameliorate glucose levels of patients.16

METHODS

Existing study is a descriptive analytic cross-sectional study and it’s been done in diabetes clinic of Imam Khomeini hospital in Ardabil (Feb-2014 to May-2015). Statistical society of this study was diabetic patients who referred to diabetes clinic of Imam Khomeini hospital for chemotherapy. (Sampling census method was done until the completion of sample size). Sample size was determined 186 individuals by following formula with test ability of 80%, confidence level of 95%, error of 5% and diabetes prevalence of 6%.17

\[ N = \left( \frac{Z_α/2 + Z_β}{P} \right)^2 \times P \times Q / d^2 \]

\[ Z_{α/2} = 1.96, \quad Z_β = 0.85, \quad P = 0.06, \quad Q = 0.94, \quad d = 0.05, \quad \text{Power} = 80\% \]

Exclusion criteria’s in this study are unwillingness of patients for cooperating, having underlying diseases, being smoker and consuming nutritional supplements. In this study 186 patients with diabetes type 2 who were having chemotherapy were selected. After blood sampling patients, the levels of HbA1C (measurement with HPLC method), TG, cholesterol, HDL, LDL, Cr and vitamin E (measurement with Eliza method) were measured. And by considering patients; HbA1C they were divided through two groups: less than 7 (controlled group) and more than 7 (uncontrolled group). Food consumption of patients were asked for 3 times a week (2nd and 3rd times were reminiscent) to check the food frequency and after entering the amount of daily consumed food to N4 food analysis program. Amounts of calorie, protein and etc. in consumed food were calculated. The calculated numbers were divided by 3 and the resulted numbers showed the amount of consumed food in one day (the average of 3 days in week) and the results were entered in checklists. In checklists, questions about age, gender, weight, height, length of being diabetic, living in urban or rural and diet were asked (based on a standard questionnaire) and patient’s information with measured levels of vitamin e entered checklist and eventually data were analyzed. After data being collected, they were coded and entered SPSS V16 statistical software. After wards, after using analytical statistical methods such as t-test and Pierson statistical exam, data were analyzed with descriptive statistical methods. In all mentioned tests, test error significance for confidence level was 0.95 less than 0.05. For obeying principles of medical ethics, information was maintained confidentially and results were reported without mentioning names. Patient’s unwillingness of cooperating in performing tests, high costs of tests and overdosing vitamin supplements by patients were the restrictions of study.

RESULTS

In the existing study 186 diabetic patients were examined. From within examined patients, 129 (69.3%)
were women and the rest were men and average patients age were 53.33±11.2. From 186 patients, 158 (84.9%) were burgess and 28 (15.1) were rural and 171 patients (91.9%) were from Ardabil. Results showed that most of the patients (114 individuals) (61.3%) have used only insulin to control their blood sugar. 90 patients (48.4%) had history of using lipid lowering drugs and the rest (51.6%) didn’t. Results showed that 144 patients (77.4%) had positive diabetes type 2 in family history. And 2 patients (1%) had a history of diabetes type 1 and average period of time for being diabetic in patients were 8.4±6.6. Also patients BMI average was 28.32±4.1 (kg/m²). Results showed that average levels of blood sugar in patients were 217.5±100.5 mg/dl. The least blood sugar level was 60 mg/dl and highest was 846 mg/dl. Average of HBA1C levels of patients was 8.95±2.2. The least HBA1C level was 5 and the highest was 18.1. Cholesterol, triglyceride, HDL, and LDL levels were mentioned in Table 1 below.

<table>
<thead>
<tr>
<th>Test</th>
<th>Cholesterol (mg/dl)</th>
<th>Triglyceride (mg/dl)</th>
<th>LDL (mg/dl)</th>
<th>HDL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>198.3±49</td>
<td>195.1±107.24</td>
<td>106.05± 43.5</td>
<td>49.32± 14.90</td>
</tr>
<tr>
<td>Variance</td>
<td>2400</td>
<td>132.2</td>
<td>345.2</td>
<td>222.2</td>
</tr>
<tr>
<td>Variation range</td>
<td>291</td>
<td>676</td>
<td>230</td>
<td>86</td>
</tr>
<tr>
<td>Minimum scores (mg/dl)</td>
<td>55</td>
<td>40</td>
<td>50</td>
<td>16</td>
</tr>
<tr>
<td>Maximum scores (mg/dl)</td>
<td>346</td>
<td>716</td>
<td>230</td>
<td>102</td>
</tr>
</tbody>
</table>

Table 2: Results of liver enzymes in patients with diabetes.

<table>
<thead>
<tr>
<th>Test</th>
<th>ALT(IU/l)</th>
<th>AST(IU/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of samples</td>
<td>186</td>
<td>186</td>
</tr>
<tr>
<td>Mean(IU/l)±SD</td>
<td>25.78±16.02</td>
<td>26.64±17.2</td>
</tr>
<tr>
<td>Variance</td>
<td>256.6</td>
<td>259.8</td>
</tr>
<tr>
<td>Variation range</td>
<td>137</td>
<td>172</td>
</tr>
<tr>
<td>Minimum scores (IU/l)</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Maximum scores (IU/l)</td>
<td>141</td>
<td>177</td>
</tr>
</tbody>
</table>

Table 3: Results of calories, protein and fat intake in patients with diabetes.

<table>
<thead>
<tr>
<th>Test</th>
<th>Calories (KJ)</th>
<th>Protein (g/l)</th>
<th>Fat(g/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of samples</td>
<td>186</td>
<td>186</td>
<td>186</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>1605.4±432.4</td>
<td>81.15±72.9</td>
<td>55.8±25.67</td>
</tr>
<tr>
<td>Variance</td>
<td>7769.6</td>
<td>5316.2</td>
<td>658.9</td>
</tr>
<tr>
<td>Variation range</td>
<td>2090</td>
<td>995.6</td>
<td>151</td>
</tr>
<tr>
<td>Minimum scores</td>
<td>980</td>
<td>4.4</td>
<td>12</td>
</tr>
<tr>
<td>Maximum scores</td>
<td>3070</td>
<td>1000</td>
<td>163</td>
</tr>
</tbody>
</table>

Table 4: level Average of parameters in controlled diabetic patients and with patients of uncontrolled diabetes.

<table>
<thead>
<tr>
<th>level average of parameters</th>
<th>Mean±SD</th>
<th>Controlled diabetic patients (n=97)</th>
<th>Uncontrolled diabetic patients (n=89)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin E</td>
<td>1548.4±777.3</td>
<td>1423.4±583</td>
<td></td>
<td>0.214</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>194.6±43.87</td>
<td>202.3±53.99</td>
<td></td>
<td>0.284</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>179.9±94.17</td>
<td>211.7±118.2</td>
<td></td>
<td>0.046</td>
</tr>
<tr>
<td>LDL</td>
<td>107.9±39</td>
<td>103.9±48.18</td>
<td></td>
<td>0.538</td>
</tr>
<tr>
<td>HDL</td>
<td>48.4±14.3</td>
<td>50.3±15.6</td>
<td></td>
<td>0.362</td>
</tr>
<tr>
<td>Food Glucose</td>
<td>4.06±3.92</td>
<td>4.3±3.5</td>
<td></td>
<td>0.65</td>
</tr>
<tr>
<td>Food Protein</td>
<td>88.66±97.5</td>
<td>72.96±26</td>
<td></td>
<td>0.143</td>
</tr>
<tr>
<td>Food Fat</td>
<td>56.45±26.8</td>
<td>55.13±24.4</td>
<td></td>
<td>0.728</td>
</tr>
<tr>
<td>Food Weight</td>
<td>1292.8±326.8</td>
<td>1260.6±348.9</td>
<td></td>
<td>0.51</td>
</tr>
</tbody>
</table>

Results showed that Average Levels of vitamin E in patients, 692.2±1488.6 (nmol/l), and the lowest level of 114.4 nmol/l and the maximum level was 6235 nmol/l. Also Average levels of ALT and AST was ALT
25.78±16.2 IU/L and mean levels of AST in patients 26.64±17.2 IU/L (Table 2).

The level of calories, protein and fat patients are given in Table 3.

Also average of received vitamin E in diabetic patients food was 4.53±4.24 nmol/l. Patients’ average received food weight was 1277.4±337.01 gr. Patients were divided in two groups based on HBA1C level, first group was equal or less than 7 (controlled) second group was more than 7 (uncontrolled). At this point, 97 of the patients were controlled (52.2%) and the rest of the diabetic was uncontrolled.

Results showed that there wasn’t any significant difference between vitamin E level and cholesterol level within controlled diabetic patients and uncontrolled diabetic patients. This study showed that average of triglyceride is higher in uncontrolled group and by considering that, this difference was statistically significant (p=0.046), analysis have shown that there isn’t any significant difference between LDL levels within controlled diabetic patients and uncontrolled diabetic patients (p=0.538) and also difference between HDL levels in uncontrolled patients are higher than HDL levels in controlled patients but this difference is not statistically significant. On the other hand results showed that average of food glucose (gr/kg) in uncontrolled group is higher than control patient. But this difference was not also statistically significant and average of protein levels in food is higher in controlled patients comparing to uncontrolled patients but this difference wasn’t statistically significant either and average of food fat levels and weight is lower in uncontrolled diabetic patients comparing to control patient but this difference also wasn’t statistically significant by considering this fact that significance level of test error for confidence level was 0.95 out of 0.66 and it was more than 0.05, so it could be said that there is no link between vitamin e and food vitamin e levels.

Table 5: Results of Pearson correlation coefficient to determine correlation between levels of vitamin E, and food vitamin E.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Level of Vitamin E</th>
<th>Level of food Vitamin E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of Vitamin E</td>
<td>Pearson correlation coefficient</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Significance level</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Number of samples</td>
<td>186</td>
</tr>
<tr>
<td>Level of food Vitamin E</td>
<td>Pearson correlation coefficient</td>
<td>0.032</td>
</tr>
</tbody>
</table>

DISCUSSION

Vitamin E is one of the anti-oxidant vitamins which are being reduced by eliminating free radicals. Escalation of plasma glucose and glycemic index can increase oxygen free radicals. Therefor it’s likely that vitamin E levels in diabetic patients are lower than healthy individuals and in individuals with weak blood sugar control it’s lower than low glycemic diabetic patients.\(^5\) In the existing study it was observed that there wasn’t any direct link between cholesterol (p=0.284), HDL (p=0.362) and LDL (p=0.538) levels and blood sugar control. But in uncontrolled diabetic patients triglyceride levels were significantly higher individuals with blood sugar control (p=0.046). In a study of Taheri et al serum total cholesterol, triglyceride and LDL in diabetic patients were higher than control group but HDL serum level were lower than control group.\(^20\) This diversity was more significant about triglyceride. In a study of Esteghamat\(^8\) I and et al.\(^21\) blood glucose level glycosylated hemoglobin, total cholesterol, triglyceride and LDL-C had a significant rise in type 2 diabetic patients but HDL-C was decreased. In a study of Ahmad and et al it was observed that LDL and VLDL levels in diabetic patients were higher than health individuals (p<0.001). And also HDL levels in diabetic patients were lower than control group (p<0.001). In a study of Sawant and et al\(^22\) it was observed that FBG and HBA1C levels in diabetic patients without any neuropathy were lower than in diabetic patients with neuropathy (p<0.05). In a study of Gazis and et al.\(^23\) it was observed that in diabetic patients HBA1C (6.9 vs. 4.8, p<0.01) and systolic blood pressure (145 vs 130, p<0.01) levels were significantly divers but diastolic blood pressure levels was not different comparing to healthy individuals.

In the existing study average vitamin e levels in patient s are 1488.6±692.2 nmol/l and lowest is 114.4 nmol/l and highest is 6235 nmol/l. Also data analysis indicate that there isn’t any significant difference in vitamin e levels between diabetic controlled patients and uncontrolled patients (p=0.214), in the study of Esteghamathami et al vitamin e and c levels in diabetic patients plasma didn’t change at all comparing to control group, although vitamin e to cholesterol ratio decreased (p<0.05).\(^21\) In a study of Srivatsan et al it was observed that vitamin e level in control group was 1.08 mg/dl, in diabetic patients with side effects was 1.19 mg/dl and in diabetic patients without side effects was 1.17 mg/dl and also there wasn’t any significant diversity between vitamin e levels and studied group (p=0.64).\(^24\) In a study of Ahmad et al it was observed that vitamin e and c levels in diabetic individuals were lesser than control group (p<0.001) and there wasn’t any significant diversity in vitamin a levels between two groups.\(^5\) In a study of Onyesom et al it was observed that vitamin a (14.38 microgram/l), vitamin c (0.66 mg/dl) and vitamin e (0.51 mg/dl) level in recently
diagnosed diabetic patients were lesser than control (healthy) group’s individuals (p<0.05).17 Diabetic patients have about 30% vitamin a deficiency, 36% vitamin c deficiency and 12% vitamin e deficiency. In a study of Sawant et al it was observed that vitamin e level in diabetic patients without neurologic side effects is 1153 and in diabetic patients with neurologic side effects (neuropathy) is 730 and this diversity was statistically significant (p<0.05).22

In a study of Salonen and et al after patient follow up and also measurements of vitamin e in them, it was observed that vitamin e deficiency can increase the diabetes risk to 3.9 times.22 Decrease in vitamin e serum density about 1 mumol/l, can increase diabetes risk about 22%. In a study of Dogon and et al it was observed that vitamin e and c levels in diabetic patients were significantly lesser than individuals of control group.22 In a study of Dosoo and et al it was observed that antioxidant status in diabetic patients with the receiver of sugar lowering tablets (NIDDM) was significantly lower than healthy individuals (p<0.001).26 Also it was observed that with the increase in fasting glucose, anti-oxidant levels decreased significantly. Good control of fasting glucose in patients resulted in decrease in free radicals. And increase in antioxidant levels.

In a study of Odum and et al.27 it was observed that average of total antioxidant (1180 micromol/l), vitamin c (26.59 micromol/l) and vitamin e (1533 micromol/l) in diabetic patients were significantly lower than healthy individuals (in all cases p=0.0001) in a study of Lapolla and et al it was observed that vitamin e level and total antioxidant status in diabetic patients with peripheral arterial disease (ABI<0.9) were lower than diabetic patients without periphrar arterial disease.28

In the most of the studies among them in Baliarsingh et al, de Oliveira et al, Baolissi et al and also in park and et al vitamin e deficiency in diabetic patients was lower comparing to control patients and this low deficiency was considered as a risk factor (OR>1).29,32 In a study of Ble Castillo and et al this vitamin again was higher in diabetic patients comparing to healthy individuals and these high levels were considered as a protection factor (OR<1).33 In the other studies among them in Reaven et al and also Economides and et al the vitamin levels were not significantly different in both groups and also both groups’ diabetic individuals were almost as same as non-diabetic individuals.34,35

After studying several related researches it was observed that the most of them were about studying vitamin e levels in diabetic patients and health individuals. So by considering this vitamin e levels in most of the studies vitamin e levels in diabetic patients were significantly lower than healthy individuals. But in this study thence vitamin e levels were controlled or uncontrolled in diabetic patients. These vitamin levels were not significantly different. Also in most of the researches vitamin e effect on diabetic patients was studied. For example in a study of Khabbaz et al it was observed that vitamin e prescription can decrease FBS (fasting blood sugar) and triglyceride but however this de-escalation was not significant.36 Total cholesterol, systolic and diastolic blood pressure levels didn’t change significantly. In the study of Vieira and et al it was observed that treatment with alpha tocpheol can cause de-escalation in systolic hypertension and LDL and also escalation in HDL levels but it cannot significantly change triglyceride and total cholesterol levels.37 In the study of Gazis and et al it was also observed that vitamin e prescription cannot cause vasodilation in diabetic patients.23 In the study of Paolisso et al it was observed that long term vitamin e prescription can lower plasma glucose (p<0.05), triglyceride (p<0.02), free fatty acids (p<0.05), total cholesterol (p<0.05), LDL (p<0.04), HbA1C (p<0.05) and apportion B (p<0.05) but however it couldn’t lower insulin resistance.31

In the study of Khabbaz et al it was observed that vitamin e prescription with 800 units in a day for 3 month cannot ameliorate blood sugar, blood fat, glycolised hemoglobin levels, fasting insulin and blood pressure in type two diabetic patients.36 In the study of Lonn and et al it was observed that daily prescription of 400 unit’s vitamin e has absolutely no effect on decreasing the possibility of cardiovascular diseases in diabetic patients.38

In the study of Boshtam and et al it was observed that daily prescription of 200 unit’s vitamin e in diabetic patients caused an insignificant de-escalation in FBS levels and insulin resistance.39 The prescription of the vitamin also couldn’t make a change in triglyceride and total cholesterol levels.

In the study of Susomboon and et al.36 which was a systemic study/ it was observed that in 9 studies, vitamin e supplements couldn’t decrease blood sugar levels in diabetic patients. also it was observed that vitamin e decreased blood sugar in patients with uncontrolled blood sugar (HbA1C>8%) and also this vitamin was lower in patients with uncontrolled blood sugar (HbA1C>8%). The results of these researches indicate that vitamin e prescription does not have significant effect on lowering diabetes side effects. By considering achieved results from existing research, it has been suggested that by considering insignificant diversity in both controlled and uncontrolled diabetic groups and also similar studies which have been done in other countries to not to prescribe antioxidant vitamins such as vitamin e unreasonably and without indications due to unaffordability and also patients non-compliance for taking too much drugs. And the prescription of these kinds of drugs should be only limited to specify indications such as triglyceride, fatty liver and etc. but of course this needs more research too. In this study health individuals’ group was not studied as a control group. Hence in comparing to the most of the studies which had
control group we couldn’t do a good comparison by vitamin e levels significance. In this study vitamin c and other antioxidants were not studied.

CONCLUSION

Results of existing study indicated that there is absolutely no significant diversity between controlled and uncontrolled diabetic individuals in vitamin E levels.

ACKNOWLEDGEMENTS

Thus, the authors are thanked of all staff and patients in Imam Khomeini hospital that cooperated in this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES
