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Effect of vitamin C on blood glucose, serum lipids & serum insulin in type 2 diabetes patients

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***Background & objectives*: Diabetes mellitus is one of the most common metabolic disorders that causes micro- and macro-vascular complications. Because of additive effects of hyperglycaemia and hyperlipidaemia for cardiovascular diseases, lipid abnormalities should be evaluated in diabetes. As vitamin C is known for its beneficial effects on serum lipids and glycated haemoglobin (HbA_{1c}), we evaluated the effect of different doses of vitamin C on blood glucose, serum lipids and serum insulin in individuals with type 2 diabetes mellitus.**

***Methods*: A total of 84 patients with type 2 diabetes referred to Yazd Diabetes Research Center, Iran, were included in the study. They received randomly either 500 mg or 1000 mg daily of vitamin C for six weeks. Fasting blood sugar (FBS), triglyceride (TG), total cholesterol (TC), low and high density lipoprotein (LDL, HDL), glycated haemoglobin HbA_{IC} and serum insulin were measured before and after vitamin C consumption and the results were analyzed.**

***Results*: A significant decrease in FBS, TG, LDL, HbA_{1c} and serum insulin was seen in the group supplemented with 1000 mg vitamin C. The dose of 500 mg vitamin C, however, did not produce any significant change in any of the parameters studied.**

***Interpretation & conclusions*: Our results indicate that daily consumption of 1000 mg supplementary vitamin C may be beneficial in decreasing blood glucose and lipids in patients with type 2 diabetes and thus reducing the risk of complications.**

Key words Insulin - lipid - type 2 diabetes - vitamin C

Vitamin C is an important antioxidant in human[1], capable of scavenging oxygen-derived free radicals[2]. Vitamin C is structurally similar to glucose and can replace it in many chemical reactions, and thus is effective in prevention of non-enzymatic glycosylation of proteins[3]. In addition, vitamin C acts as a regulator of catabolism of cholesterol to bile acid in guinea pig and has been demonstrated to be an important factor in lipid regulation[4]. Ness *et al*[5] showed beneficial effects of vitamin C on lipids in human.

Several studies showed decreased basal vitamin C level in diabetic patients[6,7] and also it is suggested that oxidative stress is increased in diabetes[2,8,9]. Most patients with diabetes have lipid metabolism disorders;

most prevalent forms are decreased high density lipoprotein (HDL) and increased triglyceride[10]. High doses of ascorbic acid (2 g/day) have been shown to improve blood glucose regulation and reduce serum cholesterol and triglyceride in type 2 diabetes patients[11].

Sargeant *et al*[12] found an inverse relationship between plasma vitamin C and glycated haemoglobin (HbA_{1c}) levels, in such a way that mean plasma vitamin C was significantly higher in individuals with HbA_{1c} < 7 per cent than in those with self reported or prevalent undiagnosed hyperglycaemia (HbA_{1c} > 7%).

We undertook this study to evaluate the effects of vitamin C supplement on blood sugar, insulin, serum lipids and levels of HbA_{1c} in patients with type 2 diabetes.

Material & Methods

This study was performed at Yazd Diabetes Research Center, Yazd, Iran during June 2005 - August 2006 as a randomized controlled trial and with parallel design. From 500 type 2 diabetic patients visited the centre, a total of 84 subjects whose fasting blood sugar (FBS), triglycerides (TG) and cholesterol levels were in the ranges that did not need to change their treatment plan, were selected by simple random sampling method. We used treatment plan, selected by simple random sampling method. American Diabetes Association (ADA) criteria were used for diagnosis of diabetes[13]. Patients with complications of diabetes including nephropathy (84 patients), retinopathty (78 patients), history of renal stones (2 patients), hypoglycaemia (8 patients), blood glucose higher than 250 mg/dl (101 patients), serum levels of triglycerides >400 mg/dl (62 patients), total cholesterol >400 mg/dl (34 patients) and who were on insulin therapy (83 patients), were excluded from the study.

Following values were considered normal; FBS < 126 mg/dl[13], triglyceride ≤ 200 mg/dl, total cholesterol < 200 mg/dl, HDL-cholesterol > 35 and LDL-cholesterol < 100[14]. Age, sex, weight, height (and calculated BMI), duration of diabetes, blood pressure (BP) were examined and recorded. Blood samples (5000 µl) were drawn from the patients and FBS, total cholesterol (TC), LDL, HDL, TG, HbA_{1c} and serum insulin were measured before the initiation of supplementation with vitamin C. HbA_{1c} was measured by ion-exchange chromatography using DSS Pink-300 test kit (Drew Scientific Limited, UK) from whole blood immediately after obtaining the sample. Insulin concentrations were detected using a human ELISA test kit (Q-1-DIAPLUS, USA) after the serum samples were thawed at room temperature. This assay had a sensitivity margin of 0.5 µU/ml.

Subjects enrolled in the study received randomly either 500 mg (group A) or 1000 mg (group B) of vitamin C (two or four tablets containing 250 mg of vitamin C, a product of Zahravi Pharm. Co., Iran) daily for six weeks. The treatment, diet and physical activity of the patients remained unchanged during the course of study. Patients' compliance to the prescribed drug was monitored by a dairy checklist and continuous contact by phone.

After six weeks of supplementation with vitamin C, patients were examined again and the tests repeated.

This study was approved by the medical ethics committee of Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran. All patients were informed about the study and a written consent was taken from all participants.

Statistical analysis: The data were analyzed statistically by SPSS for Windows (version 11.5). Statistical methods used were Chi-square, paired T-test, and ANOVA. $P<0.05$ was considered significant.

Results & Discussion

Mean age of 84 patients (43 male, 41 female) was 52.3 ± 9.62 yr (range: 33-75 yr). Of these, 41 (19 men and 22 women) patients underwent treatment with 500 mg (group A), and 43 (24 men and 19 women) received 1000 mg of vitamin C (group B). Mean duration of disease was 7.62 ± 5.74 yr (ranged from 1-27 yr). Statistical analysis did not show any differences between the two groups in the age, sex and duration of diabetes.

Also, there were no significant differences in systolic blood pressure, body mass index (BMI), TC, LDL, TG, HbA_{1c} and serum insulin levels between the two groups before treatment but diastolic blood pressure ($P<0.05$) and HDL($P<0.001$) were significantly different. Consumption of 1000 mg vitamin C (group B) resulted in significant changes in serum levels of FBS, TG, LDL, HbA_{1c} and insulin ($P<0.05$ & <0.001), but supplementation of 500 mg vitamin C did not result in any changes in these parameters. There was no significant change in the serum levels of TC and HDL in both the groups (Table).

In our present study, we compared two doses of vitamin C (500 mg versus 1000 mg) that showed a

Table. Mean values of FBS, lipid profile, HbA_{1c} and insulin before and after supplementation with different doses of vitamin C (Data are mean ± SD)

	Group A (n = 41)		Group B (n = 43)	
	Before treatment	After treatment	Before treatment	After treatment
FBS (mg/dl)	152.68 ± 34.54	159.32 ± 40.32	169.33 ± 34.02	144.80 ± 33.44**
TG (mg/dl)	202.66 ± 55.1	201.68 ± 51.4	210.02 ± 65.1	186.56 ± 54**
TC (mg/dl)	191.78 ± 34.7	190.05 ± 36.8	198.28 ± 38.1	187.72 ± 31.2
LDL (mg/dl)	127.93 ± 40.1	124.85 ± 39.1	130.95 ± 35.5	125.91 ± 33.8**
HDL (mg/dl)	36.83 ± 9.1	38.37 ± 8.8	45.86 ± 11.1	47.77 ± 10.6
HbA_{1c} (%)	8.36 ± 1.7	8.41 ± 1.6	8.82 ± 1.3	7.66 ± 1.3**
Insulin (μU/ml)	10.40 ± 2.4	10.98 ± 2.4	16.91 ± 3.1	8.77 ± 1.3*

*P**<0.05 ***<0.001 compared to before treatment
FBS, fasting blood sugar; TG, triglycerides; TC, total cholesterol; LDL, HDL, low and high density lipoprotein; HbA_{1c}, glycated haemoglobin

significant reduction in serum FBS, LDL, HbA_{1c} as well as serum fasting insulin after consumption of 1000 mg/day of vitamin C. In our previous studies as a clinical trial (before and after) we showed a significant decrease in FBS, LDL and HbA_{1c} levels after usage of 1000 mg of vitamin C in type 2 diabetic patients[3,15]. In a study by Chen *et al*[16], daily consumption of 800 mg ascorbic acid for 4 wk by type 2 diabetes patients caused no significant changes in FBS and serum insulin. This may be due to lower dose used compared to our study. Forghani *et al*[17] showed a significant decrease in serum HbA_{1c} and LDL levels in patients supplemented with 1000 mg/day of vitamin C for 6 wk. In our study, 1000 mg/day dose of vitamin C did not cause significant fall in serum TC while Errikson *et al*[11] in Finland using 2 g of vitamin C for 90 days, showed a significant decrease in TC. This difference may be due to a higher dose used by them.

LDL particles are small and dense in type 2 diabetes and are susceptible to oxidation. α-tocopherol is a lipid soluble antioxidant and protects LDL particles from oxidative attack. Vitamin C is required for regeneration of α-tocopherol and may thus prevent LDL oxidation[18].

In another study performed by Bishop *et al*[19] on 50 hyperlipidaemic diabetes patients, supplementation with 500 mg/day vitamin C resulted in no changes in FBS, TC, TG and HbA_{1c} in comparison with placebo. In a placebo-controlled study done by Paolisso *et al*[20] on 40 elderly type 2 diabetes patients, supplementation with 500 mg vitamin C twice daily for 4 months reduced the plasma levels of LDL, TC, TG and insulin significantly.

Endothelial dysfunction is a hallmark of type 2 diabetes related to hyperglycaemia and oxidative stress. This endothelial dysfunction may worsen insulin resistance[16]. It may be possible that vitamin C as an antioxidant can probably reduce insulin resistance by improved endothelial function and lowering oxidative stress.

In conclusion, supplementation with 1000 mg/day of vitamin C in addition to the normal diet and treatment schedule may help in improving plasma glucose and lipid profile in patients with type 2 diabetes.

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