Effect of Vitamin C Supplementation on Postprandial Oxidative Stress and Lipid Profile in Type 2 Diabetic Patients

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Abstract: Diabetes mellitus is one of the most wide spread endocrine disorders and an important developing health problem in the world. Cardiovascular disease is a common complication of type 2 diabetes. Several risk factors for coronary heart disease cosegregate in type 2 diabetes, including hyperglycemia, hyperlipaemia, increases production of free radical and decrease in antioxidant defense system. In this study we evaluated the effect of vitamin C supplementation on fasting and postprandial oxidative stress and lipid profile in type 2 diabetic patients. 30 patients with type 2 diabetes from Nader Kazemi Clinic, Shiraz, Iran were randomly divided into 2 groups; vitamin C treatment group (1000 mg d−1) and placebo group from May to September 2010. Fasting and postprandial lipid profile and Malondialdehyde (MDA) level were measured at the beginning of the study and after six weeks of supplementation. Data analysis was carried out using Mann-Whitney U test with p<0.05 being significant by SPSS software version 16. The result of the study showed a significantly decrease in fasting (p = 0.006) and postprandial MDA (p<0.001) in vitamin C group compare to placebo group but not in lipid profile. This study suggests that vitamin C supplementation can decrease fasting and postprandial oxidative stress and may prevent diabetes complication.

Key words: Type 2 diabetes mellitus, oxidative stress, vitamin C, postprandial state, Malondialdehyde

INTRODUCTION

Diabetes is one of the major endocrine disorders worldwide. It is responsible for a number of health problems and impaired quality of life. The major contributor to the increasing number of diabetic patients will be type 2 diabetes which is characterized by Excessive hepatic glucose production, decreased insulin secretion and increase insulin resistance (Rosen et al., 2001). There is emerging evidence that oxidative stress make a significant contribution in the development and progression of diabetes. Mechanisms by which increased oxidative stress involve in diabetic complication are including, oxidizing and damaging DNA, protein and lipid as well as ability to function as signaling molecules to activate the number of cellular damage (Evans et al., 2002).

Cardiovascular Diseases (CVD) mortality is high among diabetic patients due to abnormalities of plasma lipid and lipoprotein metabolism (Franz, 2004). Evidence shows that postprandial hyperglycemia and hyperlipaemia can predict cardiovascular disease risks more strongly than fasting values (Franz, 2004, Evans and Rees, 2001). It has been reported that postprandial hyperglycemia can cause endothelial dysfunction which is recognized as an early process of atherosclerosis (Bae et al., 2001, 2003). The link between acute postprandial hyperglycemia and cardiovascular risk factor has been suggested to be oxidative stress (Fox and Lefèvre, 2007; Baynes and Thorpe, 1999; Feillet-Coudray et al., 1999). Oxidative stress results from an imbalance between prooxidant load and the antioxidant defense system. In diabetes, non-enzymatic protein glycation and glucose autooxidation may generate free radicals which in turn catalyses lipid peroxidation (Feillet-Coudray et al., 1999).

Postprandial increases of lipid and carbohydrate concentrations causes oxidative stress, by increasing the

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production of free radicals through activating several biochemical pathways (Ceriello et al., 1998) which has been associated with increased susceptibility of LDL oxidation (Sies et al., 2005) and a higher risk for cardiovascular disease. Evidence showed that antioxidant can provide protection from the oxidative effects of postprandial hyperglycemia and hyperlipidemia (Sies et al., 2005; Ursini and Severin, 2002; Ceriello, 2005; Tessier et al., 2009).

Vitamin C is one of the most readily available dietary antioxidants. Treatment with vitamin C inactivates the circulating free radicals (Levin et al., 2006). It has also been suggested that vitamin C exert cardiovascular and other health benefits in humans in part by acting as an antioxidant (Polidori et al., 2004). Studies have shown that vitamin C is the only antioxidant in human plasma that can completely protect endogenous lipids from detectable oxidative damage induced by aqueous peroxy radicals and other reactive oxygen species (Frei et al., 1988, 1989).

The aim of the present study was to determine the effects of vitamin C supplementation on postprandial oxidative stress and lipid profile in diabetic patients in order to decrease or prevent cardiovascular disease in this group of population.

**MATERIALS AND METHODS**

**Subjects:** A randomized single blind placebo controlled clinical trial was conducted on 30 type 2 diabetic patients (age range 30-65 years; 8 men and 22 women; having diabetes for at least 1 year). All participants were nonsmoker, receiving standard oral hypoglycemic agents, had no history or clinical evidence of overt vascular disease, acute or chronic inflammatory disease.

None of the Patients were treated with lipid lowering drugs, hormone replacement therapy and/or diuretics, β-blockers and aspirin. All subjects were fully informed of the purpose and procedures of the trial and were free to leave the trial at any time. Written informed consent was obtained from all participants. This study took place in Nader Kazemi Clinic, Shiraz, Iran, which is affiliated to Shiraz University of Medical Sciences from May to September 2010. The research protocol was approved by the Ethics Committee on Human Experimentation of Shiraz University of Medical Sciences.

Diabetic patients were randomly divided in two groups (4 men and 11 women in each group). Group 1 vitamin C treatment group (1000 mg day⁻¹). Group 2 placebo (acetate cellulose) group (1000 mg day⁻¹). All subjects received supplements and placebo for six weeks.

The supplement and placebo capsules looked identical and were specially prepared for this study by General Nutrition Center (GNC) in the USA.

We wanted from participants to avoid any changes in their medication whenever possible.

**Protocol:** Five milliliters of blood were collected after overnight fasting, for the measurement of serum total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride and malondialdehyde (MDA) level. Each participant was then given a breakfast that contained 80 g fat (include a piece of cake, a small cheese sandwich and 200 mL high fat milk) and afterwards to take a rest in a chair and watch a television without any food, tea and or coffee. Two hours after finishing the test meal Lipid profile and MDA level were measured repeatedly (postprandial state). At this point patients in group 1 received vitamin C (1000 mg day⁻¹) and group 2 received placebo (acetate cellulose) for six weeks. At the end of six weeks the baseline procedure was repeated and fasting and 2 h post-prandial lipid profile and MDA level measured.

Lipid profiles were measured by biosystem A-25 autoanalyser. Plasma MDA concentration was measured by determines levels of TBARS (Thiobarbituric acid reactive substances) as a measure of lipid peroxidation by using spectrophotometric assay.

**Data analysis:** Data analysis was carried out using Mann-Whitney U test to compare the mean differences between both groups by SPSS software version 16. Basic data expressed as Mean±standard deviation, fasting and postprandial biochemical parameters before and after intervention expressed as median (inter quartile range). It was considered significant if the p value was lower than 0.05.

**RESULTS**

Table 1 shows the general and demographic characteristics, biochemical parameters and daily doses of drug intake of the 30 diabetic patients participated in this study. Considering the parameters reported in Table 1, no
significant differences was observed in general characteristics such as sex, age, duration of diabetes, Body Mass Index (BMI), daily dose of drugs and biochemical parameters between the vitamin C and placebo groups at baseline. Three patients were excluded from statistical analysis because they interrupted trial treatment.

After six weeks of supplementation, level of MDA was significantly lower on both fasting (p = 0.006) and postprandial state (p<0.001) in patients treated with 1000 mg day\(^{-1}\) vitamin C compared to placebo. However, no significant differences were observed in the fasting and postprandial lipid profile of patients after vitamin C supplementation (Table 2).

**DISCUSSION**

This study demonstrates that supplementation of 1000 mg Vitamin C for 6 weeks can significantly decrease MDA concentration in fasting and postprandial state in diabetic patients. While this study showed the effect of vitamin C supplementation on MDA concentration of diabetic patients, others evaluate the vitamin C effect on plasma antioxidant status and resistance to lipid peroxidation of healthy subjects. Short-term and long-term vitamin C supplementation in humans significantly increases plasma ascorbate concentrations and dose-dependently improves the resistance of plasma to lipid peroxidation (Polidori et al., 2004). The finding of this study is in agreement with other studies that have shown that vitamin C effectively protecting plasma against oxidative damage (Tessier et al., 2009; Polidori et al., 2004; Frei et al., 1988, 1989).

In this study we investigated the effect of vitamin C on fasting and postprandial oxidative stress and lipid profile. Our findings suggest that supplementation of 1000 mg Vitamin C at least 6 weeks can significantly decrease MDA concentration in fasting and postprandial state in diabetic patients that was in agreement with other studies (Tessier et al., 2009; Polidori et al., 2004; Frei et al., 1988, 1989). We did not observe any effect of Vitamin C on fasting and/or postprandial lipid profile.

Previous studies have suggested that Diabetes is a disease in which hyperglycemia and increased Free Fatty Acids (FFA) result in generation of Reactive Oxygen Species (ROS) which are involved in the pathogenesis of diabetic complications through increased oxidative stress (Evans and Rees, 2001; Brownlee, 2001; Maxwell et al., 1997; Brownlee, 2005; Evans et al., 2003). One major consequence of this process is the production of gene products such as pro-inflammatory cytokines (TNF-\(\alpha\) and IL-6) endothelin-1 (ET-1) and adhesion molecules which are associated with endothelial dysfunction (Park et al., 1999). Furthermore, free radicals are able to damage lipids through lipid peroxidation that is strongly contributed to the development of atherosclerosis (Rosen et al., 2001).

Recent evidence showed that the postprandial hyperglycemia and hyperlipaemia is an important contributing factor to the development of atherosclerosis (Bonora and Muggeo, 2001). In diabetes, the postprandial phase is characterized by a rapid and large increase in blood glucose and Triglyceride (TG) rich lipoprotein (Ceriello, 2005; Kusunoki et al., 2000). It has been suggested that over generation of oxidative stress due to hyperglycemia and hyperlipidemia in diabetic patients, induce an endothelial dysfunction (Ceriello et al., 2002). Our study reaffirms that type 2 diabetes is associated with oxidative stress. Other studies showed a postprandial increase in a product of oxidative damage (MDA), closely mirroring the changes in blood glucose in diabetic patients (Temelkova-kurtschiev et al., 2000).
Thus, postprandial hyperglycaemia and hypertriglyceridaemia may act as predictors of CVD in diabetic patients (Teno et al., 2000).

Temelkova-Kurttschiev et al. (2000) showed that diabetes mellitus alters the antioxidant defense system. There is also evidence that treatment with vitamin C may reduce the oxidative stress production (Evans et al., 2003) and so improving endothelial function and reduces the cardiovascular related problems (Evans et al., 2002). This study support previous observation of beneficial effects of vitamin C on oxidative Stress (Title et al., 2000; Maharjan et al., 2008; Neri et al., 2005). Our data demonstrated reduced oxidative stress production in vitamin C supplemented group as well.

In conclusion this study shows that a short time supplementation of vitamin C can significantly reduces the MDA, a major product of oxidative damage in both fasting and postprandial states of type 2 diabetic patients.

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REFERENCES


