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Biomarker Level of Oxidative Stress after Oral Supplementation of Vitamin C in Patients with Type 2 Diabetes Mellitus

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Abstract **Original Research Article**

Background: Diabetes mellitus is one of the most widespread endocrine disorders and its complications are increasing all over the world. Hyperglycemia causes excess free radicals generation leading to oxidative stress which is responsible for micro vascular and macro vascular complications. Serum malondialdehyde (MDA) level may reflect oxidative stress in type 2 DM. Vitamin C has been suggested to be an important antioxidant for scavenging oxygen-derived free radicals. ***Objective:*** To observe the effects of oral supplementation of vitamin C on biomarker level of oxidative stress in patients with type 2 diabetes mellitus. ***Method:*** From July 2015 to June 2016, a prospective interventional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka. A total of 33 diagnosed type 2 diabetic patients of both sexes with age ranging from 40 to 55 years were chosen. The study group consisted of 17 type 2 diabetic patients who received vitamin C (1000 mg/day) supplements for 6 weeks. Another 16 age-matched type 2 diabetic patients were used as a control group for comparison, with no vitamin C supplementation. All subjects in both groups were studied twice, once at the beginning of the study (baseline) and once after 6 weeks of study. ***Result:*** At the beginning of the study, the mean MDA level was almost identical, and the difference between the control and study groups was not statistically significant (baseline). The mean serum MDA level in diabetic patients was significantly ($p<0.001$) reduced after six weeks of vitamin C supplementation compared to their baseline value. Again, after 6 weeks, serum MDA level was significantly ($p=0.002$) lower in vitamin C supplemented patients compared to control group who were not supplemented with vitamin C. ***Conclusion:*** Supplementation of vitamin C is found effective in reducing the biomarker level of oxidative stress.

Keywords: Biomarker; Vitamin C; Oxidative Stress; Oral Supplementation; Type 2; Diabetes Mellitus.

I. INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels [1].

Diabetes is one of the world's most serious public health crises of the twenty-first century. According to IDF [2], diabetes mellitus affected approximately 415 million people aged 20 to 79 years, with a prevalence of 8.8 percent. This figure is steadily rising and is expected to reach 642 million by 2040, with a prevalence of 10.4%. The highest regional prevalence of diabetes was reported for North America (12.9%), followed by South East Asia (8.5%). In Bangladesh, the prevalence of diabetes mellitus was about 7.4% for the year 2015[3].

MDA is an end product of the enzymatic or nonenzymatic decomposition of arachidonic acid and larger PUFAs. The reaction of oxygen with unsaturated lipids, known as lipid peroxidation, produces a wide range of oxidation products. Lipid hydroperoxides (LOOH) are the main primary products of lipid peroxidation, and secondary products include malondialdehyde (MDA), propanal, hexanal, and 4-hydroxynonenal (4HNE). MDA appears to be the most mutagenic lipid peroxidation product. Because of its easy reaction with thiobarbituric acid, MDA has been widely used for many years as a convenient biomarker for lipid peroxidation of omega-3 and omega-6 fatty acids. Because MDA is one of the most popular and reliable markers for determining oxidative stress in

clinical situations, and due to MDA's high reactivity and toxicity, this molecule is very important to the biomedical research community[4].

In type 2 diabetes mellitus, chronic hyperglycemia leads to an increase in free radical production from glucose autoxidation, protein glycation, and glycoxidation. Excess free radicals cause lipid peroxidation, which results in oxidative stress. Diabetic complications such as diabetic nephropathy, retinopathy, neuropathy, and cardiovascular disease are caused by oxidative stress. Malondialdehyde (MDA), a byproduct of lipid peroxidation, is an excellent marker of free radical-mediated damage and oxidative stress in type 2 diabetes mellitus [5, 6].

Vitamin C is an important antioxidant in human, capable of scavenging oxygen-derived free radicals. It regenerates other antioxidant such as vitamin E, reduced glutathione, urate and ß-carotene from their respective radical species and maintains a continual antioxidant supply in the body. Therefore, it plays an important role in the prevention of oxidative damage to DNA, lipids, and proteins [7]. It also aids in the regulation of glucose levels in people with type 2 diabetes [8]. By scavenging free radicals, vitamin C improves insulin signalling and insulin-mediated glucose transport in type 2 diabetes mellitus [9]. It lowers serum glucose by preventing glycogenolysis in hepatocytes [10]. Vitamin C is an electron donor and inhibits lipid peroxidation by reduction of the reactive oxygen species [11]. Supplementation of vitamin C significantly reduces serum MDA level in type 2 diabetic patients [12, 13].

The effect of vitamin C on oxidative stress in Bangladeshi type 2 diabetes mellitus patients is poorly understood. So, the present study was intended to assess the effects of oral supplementation of vitamin C on biomarker of oxidative stress in Bangladeshi type 2 diabetes mellitus patients.

II. METHOD

From July 2015 to June 2016, a prospective interventional study was carried out at the Department of Physiology, Dhaka Medical College, and Dhaka. The control and study individuals were taken from the Dhaka Medical College Hospital's Outpatient Department of Endocrinology. At the beginning of the study, 40 diagnosed type 2 diabetic patients (ADA, 2015) aged 40-55 years of both sexes, suffering ≥3 years, having oral hypoglycemic drugs and not having antioxidant supplements in the last 4 weeks were randomly assigned to two groups equally. Participants who were pregnant, on insulin therapy, history of renal stone and renal failure, taking drugs which interact with vitamin C metabolism such as anticoagulant, barbiturates were excluded from the study.

Four patients from the control group and three patients from the study group did not return for follow-up after the six-week trial period. As a result, the study was completed by 16 subjects from the control group and 17 subjects from the study group. After selection of the subjects, informed written consent was taken from the participants. Study subjects were advised to take vitamin C supplement 1000 mg/day for 6 weeks. Both control and study groups were advised to maintain former food habit, physical activities and type and doses of medicine during the course of the study. Regular telephonic contact was made to ensure compliance with intervention. A detailed family and medical history was obtained, as well as anthropometric measurements and blood pressure measurements of the subjects.

All the information was recorded in a prefixed questionnaire. MDA level was estimated in the Department of Laboratory Services of National Institute of ENT, Dhaka. These parameters were studied twice in all subjects of control and study group, once at the beginning of study (base line) and once after 6 weeks of study period. All the parameters were expressed as mean ± SD (standard deviation). Paired Student's't' test and unpaired.

Student's 't' test were used to see the level of significance. p value < 0.05 was considered as level of significance. Statistical analyses were performed by using a computer based statistical program SPSS (Statistical package for social science) version 22.0.

III. RESULTS

Table-1: General characteristics of the subjects in both groups (n=33)

Parameters	Control group (n=16)	Study group (n=17)	p value
Age (years) Sex	47.50 ± 4.42	49.29 ± 4.95	0.282^{ns}
Male	6 (37.5)	8 (47.1)	0.841
Female	10 (62.5)	9 (52.9)	
BMI (kg/m^2)	25.79± 2.53	24.32± 2.79	0.125
Duration of DM (years)	4.68± 1.88	5.00± 2.57	0.685
Systolic BP (mmHg)	125.00± 6.32	127.05± 8.48	0.436
Diastolic BP (mmHg)	80.00± 7.07	80.58± 9.33	0.841

There were no significant differences in age, sex, BMI, duration of DM and blood pressure between two groups.

Table-2: Serum malondialdehyde (MDA) level in different groups (n=33)

Serum MDA	Control group (n=16)	Study group (n=17)	p value
At baseline	8.74± 2.27	7.98± 2.43	0.361^{ns}
After 6 weeks	8.75± 2.27	6.23± 1.95	0.002*
p-value	0.100^{ns}	<0.001***	

Serum malondialdehyde was decreased significantly in study group.

IV. DISCUSSION

The present study was undertaken to observe the effects of oral supplementation of vitamin C on biomarker level of oxidative stress in type 2 diabetic patients. A total of 33 diagnosed type 2 diabetic patients of both sexes with age ranging from 40 to 55 years were chosen for this study. The study group consisted of 17 type 2 diabetic patients who received vitamin C (1000 mg/day) supplements for 6 weeks. Another 16 agematched type 2 diabetic patients were used as a control group for comparison, with no vitamin C supplementation. All subjects in both groups were studied twice, once at the beginning of the study (baseline) and again after 6 weeks of study.

In this study, the mean age and BMI of the study subjects in both the control and study groups were nearly identical, with no statistically significant differences observed between them. The mean systolic and diastolic blood pressures, as well as the duration of disease, were nearly identical in both groups.

At the beginning of the study, the mean MDA level was almost identical, and no statistically significant difference was observed between the control and study groups (baseline). Almost identical findings were observed by various investigators from various countries [12, 14].

Serum MDA level in diabetic patients was significantly (p<0.00l) lower after 6 weeks of vitamin C supplementation compared to their baseline value but no significant (p=0.100) changes was found in control group in MDA level than that of their baseline value. Again, after 6 weeks, serum MDA level in patients supplemented with vitamin C was significantly (p=0.002) lower than that of diabetic control group who were not supplemented with vitamin C. Almost identical types of results were observed by researchers from various countries [12, 13]. On the other hand, Kebapci *et al*. [15] and Tessier *et al*. [14] discovered no significant difference in serum MDA level in patients after vitamin C supplementation.

V. CONCLUSION

Vitamin C administration in regular doses improved biomarker level of oxidative stress in type 2 DM patients.

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