Correlation of Selenium and other antioxidants in diabetic patients with and without complications

Robby Kumar

Department of Biochemistry, SSR Medical College, Mauritius

ABSTRACT

Background: Diabetes mellitus causes free radicals generation which is one of the major causes for the complications in diabetes mellitus. **Objective:** To investigate whether selenium level differs between Type 2 diabetic subjects with and without complications and correlate with antioxidant status. **Methodology:** Subjects were divided into group-I-Diabetics without any complications and Group-II-Diabetics with complications. Serum Glucose, Lipid Profile, Selenium was estimated along with reduced Glutathione, Superoxide dismutase and Thiobarbituric acid reacting substances in both the groups and they were compared with healthy controls. **Results:** Serum selenium and other markers of oxidative stress were found to be statically decreased in both the groups when compared with control. **Conclusion:** there is a significant reduction in selenium in serum as the disease progresses; hence reduced selenium indicates metabolic response towards the oxidative stress in patients with diabetes. Thus, selenium can be used in diabetics to prevent late complications.

Keywords: Antioxidants, Diabetes mellitus, Selenium, Lipid Peroxidation

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder which is widespread and is associated with substantial morbidity and mortality. It causes cardiovascular disease, nephropathy, neuropathy, retinopathy and other complications that affect severely the quality of life in later stages. The basis of these chronic complications is attributed to inability of pancreatic cells to produce insulin or by resistance towards insulin action. Diabetes is usually accompanied by increased free radical production[1] or impaired antioxidant defences[2]. Increased free radicals causes' damage to cellular proteins, membrane lipids and nucleic acid and finally cell death. Free radicals are generated due to- glucose oxidation which produces superoxide anion radicals[3], hyperglycemia which promotes lipid peroxidation[4], Advanced Glycated End (AGE) products[5] and finally by sorbitol pathway which leads to NADPH and Glutathione depletion[6]. In diabetes mellitus hyperglycemia not only increases free radicals formation but also impairs Antioxidant defense mechanism[7]. It is now known fact that increased superoxide formation after high glucose–induced throughout in the mitochondrial electron-transport chain which leaks reactive oxygen species, involved in the development of diabetic complications[8,9]. There are numerous defense mechanisms in the body, with enzymatic and non-enzymatic constituents[10,11]. Selenium is a trace element and main constituent of soil. The demand for selenium in healthy individual is very small, where it acts mainly as an antioxidant and stops cellular damage by reactive oxygen species. Glutathione peroxidase an important enzyme that catalyses the decomposition of reactive oxygen species is a selenium-dependent enzyme, which protect the membrane lipid and haemoglobin against oxidation by peroxides[12,13,14,15,16]. Selenium not only modulates the cellular response but it also protects against oxidative stress and the production of reactive oxygen species[11,15,17]. In addition, selenium has a synergistical action with tocopherol[18,19]. Selenium and Vitamin E act as complementing each other's function against oxidative stress[20,21,22]. The existing literature data regarding the role of serum selenium levels to diabetes and its complications are controversial we conducted the present study in order to investigate whether selenium levels differ between Type 2 Diabetic subjects with and without complications.

Address for correspondence:
Robby kumar, Department of Biochemistry,
SSR Medical College, Mauritius
E-mail: kumarrobby@gmail.com

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METHODOLOGY

Subjects selected between age 40-60 years; subjects were mainly volunteers and were recruited with mutual consent. They were divided into three groups namely- Group I: 25 Normal healthy control subjects with no present or past history of diabetes mellitus; Group II: 15 Diabetics with no compactions, subjects who were freshly diagnosed from type2 diabetes mellitus was selected. Subjects taking medication or has a long past history of diabetes or any other conditions were ruled out; Group III: 20 Diabetics with complications, most of them were obese, 12 were having hypertension with nephropathy and 8 were having cardiovascular complications. Fasting Blood Samples were taken. The Blood was drawn from the forearm is mixed with 0.1 M Sodium Citrate (0.5 ml/4.0 ml of blood) and Sodium fluoride:Potassium oxalate 1:3 (w/w). The sample collected was analyzed immediately. The samples were centrifuged at 3000 g for 10 min and plasma was taken for the estimation of Blood Glucose and Lipid profile. Serum parameters were done by kit method in semi-automatic analyzer. The Red Blood Cells left were washed in cold saline and diluted hemolysates were prepared[23] for estimation of GSH (Reduced Glutahione), SOD (Superoxide Dismutase), and TBARS (Thiobarbaturic acid reacting substances). Erythrocyte GSH was estimated by method of Beutler E et.al[24]. Erythrocyte SOD was estimated by method of Beauchamp and Fridovic[25]. Along with this erythrocytic lipid peroxidation products were measured by assaying TBARS[26]. The Serum selenium was determined by atomic absorption spectrophotometer[27].

RESULTS

The serum Glucose and Lipid Profile (Total Cholesterol, Triglycerides, HDL-C and LDL-C) were normal for control and were increased for both group-II and group-III, much higher in group-III. The antioxidant status is done by measuring TBARS and GSH which was normal for control, slightly decreased in group-I but was increased in Group-II study subjects. Enzyme SOD was slightly increased in Group-I and further more increases in Group-II study subjects (Table-1). However these findings were not statically significant. Selenium values were significantly decreased in group-I and Group-II when compared with controls. A statically significant decrease of selenium values were also observed in group-II subjects when compared with group-I

DISCUSSION

As the diabetes progresses there is increased oxidative damage with subsequent reduction in antioxidant defense systems[1,2,28], which is shown here in the results, SOD, an inducible enzyme, activity is increased due to increased free radicals. GSH and TBARS are reduced in diabetic subjects, and as a compensatory mechanism they increases in group-II subjects. In diabetes, there is glycation of glutathione peroxidase resulting in functional changes of the antioxidant enzymes. Thus decreasing antioxidant status of this selenium dependent enzyme leads to more free radical production and more complication of diabetes[11,29,30]. The results obtained here are in correlation with previous findings and research is still needed to enhance knowledge in this field.

CONCLUSION

A significant reduction in selenium levels are indicators of metabolic response to oxidative stress in patient with diabetes mellitus. Though high selenium has been reported to induce diabetes mellitus[16] still it is recommended to give selenium in diabetic patient to prevent the late complications.

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Parameters	Control	Group-I	Group-II
Age	52 ± 9	55 ± 7	56 ± 9
Blood Glucose (mg/dL)	84.8 ± 12.5	196.1 ± 22.8	244 ± 39.7
TC (mg/dL)	167.1 ± 29.1	188.8 ± 12.3	290.3 ± 42.9
TG(mg/dL)	110.9 ± 24.7	142.6 ± 19.4	210.7 ± 37.6
HDL(mg/dL)	48 ± 5	44 ± 4	37 ± 8
LDL(mg/dL)	118 ± 18	129 ± 14	138 ± 21
TBARS (nM/gHb)	4.8 ± 2	3.9 ± 2	6.7 ± 4
SOD (U/gHb)	880 ± 121	986 ± 217	1080 ± 433
GSH (mg/gHb)	18 ± 4	12 ± 3	17 ± 3
Serum Selenium (microg/L)	131 ± 37.18	92.9 ± 38.1[a]	60.4 ± 31.7[b]

[a]p=0.0028 [b]p=0.005

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