Study on Serum level of Copper and Calcium in Type 2 Diabetic subjects

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ABSTRACT

Introduction*: Diabetes mellitus (DM) is a group of metabolic disorders characterized by high blood sugar level over a prolonged period of time which affects carbohydrate, lipid and protein metabolism. It causes death due to multiorgan failure. Calcium (Ca) helps in insulin secretion as it is a calcium dependent process. Excess copper (Cu) is associated with DM, increased free radical production leading to oxidative damage to various tissue and organs. This study was designed to evaluate the serum Cu and Ca status in type2 diabetes mellitus patients.* ***Methods****: This cross-sectional study was done among 60 diagnosed type 2 diabetic patients and 60 healthy people in the Department of Biochemistry, Mymensingh Medical College, Mymensingh over a period of one year from January 2015 to December 2015. Estimation of serum Cu and Ca level were done by colorimetric method by using test kits. All statistical analyses were performed by SPSS windows package, version 20. Significance of the difference between two groups was evaluated by using student's unpaired 't' test.* ***Results:*** *Study revealed that calcium levels were significantly decreased and copper levels were significantly increased in type2 diabetic patients.* ***Conclusion:*** *It can be concluded that the prevalence of decreased level of calcium and increased level of copper occurs in type 2 diabetic patients. So, in type 2 diabetic patients, calcium supplementation may be beneficial.*

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INTRODUCTION

Diabetes mellitus (DM) is probably one of the oldest diseases known to human. It was first reported in Egyptian manuscript about 3000 years ago.[1] It is aheterogeneous metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, resistance to insulin action or both. The effects of DM include long-term damage, dysfunction and failure of various organs. Diabetes can lead to kidney disease, heart disease, nerve damage and loss of vision.[2] It is one of the greatest medical problems with the worldwide explosion in its prevalence.[3] According to recent estimates the worldwide prevalence of DM is 4.2% and that indicates 150 million peoples are affected, it will

increase to 439 million by the year 2030.[4,5]

Micronutrients play crucial roles in human nutrition, regulation of metabolism (Carbohydrate, lipid and protein), heartbeat, cellular pH and bone density. People with type 2 DM has more tendency to increase morbidity and mortality due to insidious onset and late recognition, especially in poor developing countries like Africa.[6]

Copper (Cu) is an essential trace element, capable of fluctuating between the oxidized Cu^{2+} and the reduced Cu^{+} state, being co-factor for many enzymes. This divalent cation is involved in super oxide dismutase (SOD) activity. Excess copper (Cu) aggravates the hyperglycemia which causes glycation of various proteins and also displaces copper from copper binding site of protein and thus further aggravates the hypercuperemia, which lead to more oxidative damage to various tissue and organs. So, Cu through its oxidative stress, impairs the functions of islets of pancreas, leading to type 2 DM.[7]

Calcium is essential for insulin-mediated intracellular processes in insulin-responsive tissues, such as skeletal muscle and adipose tissue. It has beneficial effect on insulin action directly, by stimulating the expression of insulin receptor and thereby enhancing insulin responsiveness for glucose transport.[8,9]

Decreased calcium level in primary insulin target tissues may contribute to peripheral insulin resistance via impaired insulin signal transduction leading to decreased glucose transporter-4 activity.[10] So, Ca improves insulin sensitivity and promotes β-cell survival by directly modulating the generation and effects of cytokines.[11]

METHODS

This cross-sectional study was carried out in the Department of Biochemistry, Mymensingh Medical College, Mymensingh and the subjects were collected from the Outpatient Department (OPD) of Endocrinology, Mymensingh Medical College Hospital, Mymensingh during the period of January 2015 to December 2015. A total number of 120 subjects were studied. There were 60 cases and 60 controls. In both case and control groups male and female subjects were equally distributed (1:1). Persons having no acute complications, serious co-morbid diseases and history of renal failure were selected in both case and control groups. All study subjects were informed about the procedure and their informed written consent were taken before collection of sample. With all aseptic precautions, 6 ml of venous blood was collected from the study subjects after overnight fasting by a disposable syringe from antecubital veins. The blood was transferred to a dry screw capped sterile test tube immediately after removal of needle from the syringe with a gentle push to avoid haemolysis. Test tube was kept in vertical position until clot formation and then centrifuged at 3000 rpm for 5 minutes. Clear serum was taken out by micropipette in a plain plastic microcentrifuge tube. Estimation of serum copper and calcium were done as soon as possible by colorimetric method using test kits. In case of any delay, the sample was stored at -20 ^{0}C. Serum glucose was estimated using enzymatic method by GOD-PAP.

All statistical analysis was done by using Statistical Package for Social Science (SPSS), version-20. Results were expressed as Mean±Standard Deviation (SD). Statistical significance of reference between two groups was evaluated by using student's unpaired t test and 95% confidence limit was taken as level of significance.

RESULTS

In group 1 (case) mean blood glucose level at fasting was 9.83±1.33 mmol/L and two hours after oral glucose intake was 15.62±3.76 mmol/L, while in group 2 (control) mean blood glucose level at fasting was 4.51±0.48 mmol/L and two hours after oral glucose intake was 6.40±0.50 mmol/L respectively (Table I). In diabetic subjects, fasting and two hours after oral glucose intake, serum glucose levels were significantly higher than that of control group ($p<0.001$).

Table I: Blood glucose level in the study subject

Variables	Group 1 (Case) (Mean±SD)	Group 2 (Cotrol) (Mean±SD)	*t* value	*p* value
Fasting blood glucose (mmol/L)	9.83±1.33	4.51±0.48	29.049	$p<0.001^*$
2 hours after oral glucose intake (mmol/L)	15.62±3.76	6.40±0.50	18.842	$p<0.001^*$

Unpaired student's 't' test, *Significant

The mean serum copper levels in group 1 and group 2 were 111.37±45.19 µg/dl and 89.46±29.71 µg/dl respectively (Table II). There was significantly increased ($p<0.002$) serum copper level in group 1 compared to that in group 2.

The mean serum calcium level in group 1 and group 2 were 9.02±1.80 mg/dl and 11.33±3.03 mg/dl respectively (Table II). There was significantly decreased ($p<0.001$) of calcium in group 1 compared to that in group 2.

Table II: Serum copper and calcium level in the study subjects

Variables	Group 1 (Case) (Mean±SD)	Group 2 (Control) (Mean±SD)	*t* value	*p* value
Copper (µg/dl)	111.37±45.19	89.46±29.71	3.138	$p<0.002^*$
Calcium (mg/dl)	9.02±1.80	11.33±3.03	5.072	$p<0.001^*$

Unpaired student's *'t'* test, *Significant

DISCUSSION

It is well established that both the deficiency and possible overload of mineral micronutrients have adverse health effects. Trace elements facilitate numerous biochemical reactions, including those related to insulin and glucose metabolism.

The concentration of several trace elements have been reported to be altered in type 2 diabetes mellitus (T2DM) and these elements might have specific roles in the pathogenesis and progress of this disease.[12] This study was focused on the hypothesis that T2DM patients have an impaired levels of certain trace elements like copper and calcium. Transition metal like copper has affinity to bind with proteins that have been glycated. Generally, serum concentration of copper and ceruloplasmin is elevated in T2DM patients.[2]

In this study, serum copper level in type 2 diabetic subjects were found significantly increased ($p<0.002$) in than that of control group. The findings are consistent with the findings of Zargar et al.[13] Elevation of serum Cu level in hyperglycemic patients due to increase glycation, because of hyperglycemia and this will stimulate release of copper from copper rich compounds.[14] It is inconsistent with the findings of Prabodh et al.[15] Some other biological factors may be responsible for this inconsistency.

Calcium is important for insulin mediated intracellular processes in insulin responsive tissues, such as adipose tissue and skeletal muscle, and also necessary for insulin action. Further calcium is necessary for insulin receptor phosphorylation and proper signal transduction and that optimal GLUT-4 transporter activity.[16] This study showed a significant decrease in calcium level in T2DM patients in comparison to control group. This finding was in agreement with the result of Rooney et al.[17] The possible reason for decreasing calcium in T2DM is due to hypercalciuria.

Another study conducted by Lorenzo et al.[18] showed that there was no significant difference in calcium concentration between healthy group and patients group due to unknown cause.The results obtained from this study have clear implications regarding prediction of what biochemical changes occur in an individual patient has when he falls into type-2 diabetic disease. This speculation could persuade the treating physicians to take steps in correcting these biochemical changes, so that further progression of the disease could be delayed or nullified.

CONCLUSION

In this study, we found that serum copper level was significantly increased and serum calcium level was significantly decreased in type 2 diabetes patient. As a result it may be recommended that all type 2 diabetic patients should undergo regular checkup of serum copper and calcium level as routine test. Supplementation of calcium may be given in type 2 diabetic patient.

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