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Estimation of serum Methylglyoxal level in type 2 diabetes mellitus

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Abstract

Methylglyoxal (MG) is a highly reactive alpha-dicarbonyl and protein-bound type compound. Molecular weight of it is 72 dalton. MG binds to and modifies arginine, lysine, and cysteine residues, which leads to production of a variety of advanced glycation end products (AGEs). MG readily binds with lysine, cysteine and functionally important arginine residues of proteins. These modifications have been associated with increased risk of thrombosis and vascular disease. Methylglyoxal is derived from metabolic intermediates of carbohydrates, proteins and fatty acids. Mostly MG is derived from the metabolites of glucose and fructose metabolism that is from non-enzymatic degradation of the triose phosphate such as dihydroxyacetone phosphate and glyceraldehydes 3-phosphate. It is also produces by spontaneous fragmentation of a Schiff base during the Maillard reaction. Minor sources of MG include autoxidation of glucose and degradation of glycated proteins, oxidation of acetone in the catabolism of ketone bodies during diabetic ketoacidosis and lipid peroxidation. It is detoxified to D-lactate by reduced glutathione –dependent glyoxalase enzyme system.

We have estimated serum methylglyoxal level in patients with type 2 diabetes mellitus with and without complications. We found significant increase in methylglyoxal level in type 2 diabetes mellitus with complications as compared to control ($P<0.001$). Biochemical effects of increased MG include modification LDL, decrease the eNO and NO production and increase the risk for aggregation of lipid in arteries. MG may also increases oxidative stress, delayed wound healing, transplanted organ failure and cardiac problems, increases cGMP concentration, reduces thioredoxin and increases

inflammation. All these effects of MG may cause cardiac dysfunction, angiogenesis, ischemic reperfusion and atherosclerosis.

Key words: Methylglyoxal, Advanced glycation end products, Type 2 diabetes mellitus,

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INTRODUCTION:

Methylglyoxal (MG) is a highly reactive alpha-dicarbonyl and protein-bound type compound. Molecular weight of MG is 72 dalton (1). It binds to and modifies arginine, lysine, and cysteine residues, which leads to production of a variety of advanced glycation end products (AGEs) (1). These modifications have been associated with increased risk of thrombosis and vascular disease (2). MG is derived from metabolic intermediates of carbohydrates, proteins and fatty acids . Mostly MG is derived from the metabolites of glucose and fructose metabolism that is from non-enzymatic degradation of the triose phosphate such as dihydroxyacetone phosphate and glyceraldehydes 3-phosphate. It is also produces by spontaneous fragmentation of a Schiff base during the Maillard reaction. Minor sources of MG include autoxidation of glucose and degradation of glycated proteins, oxidation of acetone in the catabolism of ketone bodies during diabetic ketoacidosis and lipid peroxidation (3). It is detoxified to D-lactate by reduced glutathione –dependent glyoxalase enzyme system (4). Diabetes mellitus (DM) is the most common metabolic endocrine disorder in which the pancreas is unable to produce hormone insulin or insulin production is not sufficient or cells cannot effectively use this hormone (5, 6). India has become the "diabetes capital" of the world with over three crore affected patients (6). Hypoglycemia, hyperosmolar hyperglycemic state and diabetic ketoacidosis are the acute complications (3) and cardiovascular disease, nephropathy, retinopathy and polyneuropathy are the chronic complications of DM (7). The increased levels of blood glucose and ketones in people with diabetes result in elevated levels of reactive aldehyde such as MG. Increased production of MG may promote the pathology of diabetic complications (3).

MATERIALS AND METHODS:

Present study was conducted in Department of Biochemistry, Government Medical College, Miraj, Maharashtra (India). Study protocol was approved by ethical committee of Government Medical College, Miraj, Maharashtra.

Sample Size: Total 280 subjects were included in this study.

Subjects were classified into two groups

Group I: Included 140 patients with Type 2 diabetes mellitus without complications and

Group II: Included 140 patients with Type 2 diabetes mellitus with complications

The subjects having history of alcoholism, smoking, Pregnancy**,** Gestational diabetes**,** subjects declined to participate were excluded from the study.

Blood collection:

An informed consent was taken from participants after complete explanation of procedure. Blood samples were withdrawn by using stainless steel disposable needles and 5 ml polythene disposable syringe. Early in the morning after an overnight fast about 4 ml venous blood was collected from anticubital vein with aseptic precautions. Blood was collected in plain bulb, fluoride bulb as well as in an EDTA bulb for various investigations. After two hours of collection, blood samples were centrifuged at 3000 rotation per minute for 10 minutes, clear and unhemolysed serum was separated used for estimation of MG and glucose was estimated on fresh plasma. The fresh anticoagulated blood samples were used for the estimation of glycosylated hemoglobin (HbA1c).

Fasting blood glucose estimated by photometric determination of glucose based on Glucose oxidase Peroxidase (GOD POD) method (8, 9) and values were expressed as mg/dl. HbA1c estimated by Direct Enzymatic method (10, 11) and values were expressed as %. Whereas serum MG levels were estimated by using method described by Racker (12) and values were expressed as (ηmol/l). The data were evaluated statistically by using student‘t’.

DISCUSSION

We found significant increase in serum MG levels in type 2 DM with complications as compared to without complications (Table No 1).

Table No. 1: Biochemical parameters in type 2 diabetes mellitus with and without complications

Parameters	**Group I (n=140) Mean±SD**	**Group II (n=140) Mean±SD**
FBG (mg/dl)	175.4 ± 25.94	219.0 ± 24.35 *
Urea (mg/dl)	33.19 ± 5.16	51.84 ± 9.83 *
Creatinine (mg/dl)	1.01 ± 0.22	1.56 ± 0.31 *
GHb (%)	9.39 ± 1.79	12.34 ± 1.82 *
MG (ηmol/l)	197.2 ± 31.67	230.2 ± 25.92 *

This may be due to prolonged hyperglycemia. Due to prolonged hyperglycemia in diabetes mellitus, a variety of toxic α-oxoaldehydes are produced. These toxic compounds react with amino acid group of protein to produce advanced glycation end products (AGEs). In vitro studies and animal experiments in experimental diabetic models by others have suggested that MG is pathologically involved in the

progression of both macroangiopathy and microangiopathy. MG plays a major role in vascular damage to endothelial cells and in the development of hypertension, of insulin resistance and nephropathy (13). Oxidative stress promotes the formation of MG. The formation of MG and accumulation of AGEs are especially elevated in diseases characterized by hyperglycemia such as diabetes, other metabolic diseases and atherosclerosis (2). Biochemical effects of increased serum MG include modification LDL, decrease the eNO and NO production and increase the risk for aggregation of lipid in arteries. MG may also increases oxidative stress, delayed wound healing, transplanted organ failure and cardiac problems, increases cGMP concentration, reduces thioredoxin and increases inflammation. All these effects of MG may cause cardiac dysfunction, angiogenesis, ischemic reperfusion and atherosclerosis (3). In conclusion, MG is a marker of oxidative in patients with type 2 diabetes mellitus.

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