Lipid peroxidation in type 2 diabetes mellitus

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AIM: The link between hyperglycemia, enhanced free-radical activity, and the complications of diabetes is unknown. The purpose of this study is to evaluate the levels of malondialdehyde (MDA) measured as thiobarbituric acid-reactive substances (TBARS), an index of lipid peroxidation, in patients of type 2 diabetes without complications, and compare with normal subjects of the same population.

METHODOLOGY: We recruited 60 type 2 diabetic subjects without complications and with poor metabolic control and 60 age-matched controls with good metabolic control. Levels of glucose, total cholesterol, HbA_{1C}, and MDA as TBARS were determined.

RESULTS: Diabetic patients had higher levels of blood glucose (P<0.001), HbA_{1C} (P<0.001), and MDA (P<0.001) than control subjects. The total cholesterol of the control subjects and diabetic patients did not differ. There was no correlation between the family history in diabetics and elevation in either HbA_{1C} or MDA levels.

CONCLUSION: Increased levels of MDA may be a useful marker of oxidative stress. The enhanced lipid peroxidation leads to an increase in free-radical activity in type 2 diabetics. This increase in free-radical activity in type 2 diabetes mellitus along with insulin resistance can lead to activation of stress-sensitive pathways, which may play an important role in the complications of diabetes.

KEY WORDS: Lipid peroxidation, malondialdehyde, oxidative stress, type 2 diabetes.

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Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and associated with increased free-radical activity. The mechanisms of free-radical production include glucose autoxidation, protein glycation, advanced glycated end products formation, and activation of polyol pathway, ultimately resulting in oxidative stress in a variety of tissues.[1] The absence of suitable compensatory mechanisms from endogenous antioxidant systems causes a redox imbalance and leads to the activation of stress-sensitive intracellular signaling pathways.[2] Hence, oxidative stress may be implicated in the pathogenesis of diabetes.

The increased production of reactive oxygen species can lead to damage of proteins, lipids, and DNA. In addition, the activation of stress-sensitive signaling pathways that regulate gene expression can also result in cellular damage.[3]

Lipid peroxidation, owing to free-radical activity, plays an important role in the development of complications of diabetes. Although increased levels of lipid peroxidation, as a consequence of free radical activity, have been reported in both type 1 and type 2 diabetes with vascular complications;[4,5] other studies failed to detect any significant elevation in lipid peroxidation in diabetic patients,[6] probably owing to heterogeneity of the patient population. Hence, in this study, we have evaluated the levels of Malondialdehyde (MDA) measured as thiobarbituric acid-reactive substances (TBARS) (index of lipid peroxidation) in patients of type 2 diabetes without complications and poor metabolic control and compared them with normal subjects with good metabolic control and belonging to the same local population.

Methodology

The study was conducted at the Endocrinology Department of MS Ramaiah Hospital, Bangalore. The study was conducted on successive patients after informed consent was obtained from them and approved by the Ethical Clearance Committee of the institution. The study group consisted of 60 subjects (37 males and 23 females) with type 2 diabetes mellitus and 60 controls (30 males and 30 females) of age-matched normal persons.

Inclusion criteria

The diabetic patients were normotensive, without secondary causes of hyperglycemia, and on treatment with only insulin. They did not have any other complications of diabetes.

Exclusion criteria

These subjects were smokers and were taking other oral hypoglycemic agents or other antioxidant therapy.

A detailed clinical history was recorded and general physical examination was carried out on the two groups of subjects. Blood samples from the controls and the patients were drawn after an overnight fast. Fasting blood sugar was estimated by the glucose oxidase–peroxidase kit method (Accurex Biomedical Pvt. Ltd.) and total cholesterol by the end point enzymatic kit method (Accurex Biomedical Pvt. Ltd.) on a semiautomated chemistry analyzer (RA50. Ames Bayer Diagnostics India Ltd.). HbA_{1C} was estimated by the ion-exchange resin kit method (Lab-Care Diagnostics India Pvt. Ltd.). MDA was measured as TBARS by the method of Wilbur *et al.*[7]

Statistical analysis

Statistical analysis was done using student "*t*" test between the diabetic patients and controls.

Results

The clinical parameters of the controls and the type 2 diabetics are shown in Table 1; 47% of the diabetic patients had a family history of diabetes.

The fasting blood glucose, HbA_{1C}, total cholesterol, and MDA levels of control subjects and type 2 diabetics are shown in Table 2. The blood glucose levels and HbA_{1C} levels were significantly elevated in the diabetics. The increased HbA_{1C} levels (>6.5%) reflect the poor metabolic control of the patients.

Table 1: Clinical characteristics of control and type 2 diabetic subject

Diabetic patients	Control subjects	Type 2
Number	60	60
Female/male	30/30	23/37
Age (years)	22-80	23-75
Duration of diabetes		2-20
Family history		47%

Table 2: Fasting blood sugar, HbA_{1C}, MDA, and total cholesterol levels in control and type 2 diabetics

	Control subjects (*n* = 60)	Type 2 diabetic patients (*n* = 60)
FBS (mg/dl)	91.5 ± 11.9	178.7 ± 23.3[a]
HbA_{1C} (%)	5.59 ± 0.73	7.67 ± 1.0[a]
MDA (n*M*/dl)	58.9 ± 7.7	117.8 ± 15.3[a]
Total cholesterol (mg/dl)	191.0 ± 24.9	187.8 ± 24.4

**P<0.001.*

The MDA levels were significantly increased in diabetic patients. There is no correlation between the presence of family history in diabetics and elevations in either HbA_{1C} or MDA levels. There was no alteration in the total cholesterol in either of the groups.

Discussion

Diabetes mellitus has been known to be a state of excess generation of free radicals contributed by several mechanisms, including hyperglycemia and antioxidant status, causing oxidative stress. This oxidative stress exacerbates the development and progress of diabetes and its complications.

Excessive production of free radicals observed both in type 1 (insulin-dependent) and type 2 (noninsulin dependent) diabetes and its insufficient removal results in damage to cellular proteins, membrane lipids, and nucleic acids.[8] Griesmacher *et al.*[4] have shown increased lipid peroxidation owing to elevated free radicals in both type 1 and type 2 diabetes. Significantly higher levels were reported in type 2 when compared with type 1. A similar increase in lipid peroxidation has been observed in our study on type 2 diabetics without secondary complications, but with poor metabolic control. Turk *et al.*[9] have, in addition, shown an increase in superoxide dismutase activity and decrease in catalase activity and suggested that these alterations may be owing to the compensatory mechanisms of the antioxidant system in type 2 diabetics.

In type 2 diabetes, which is associated with insulin

resistance, there is an increase in free-radical production and prevention of the development of the typical secondary complications would require strategies to normalize free-radical production.

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