Relationship between malondialdehyde activity (MDA) & Lipid Profile in Diabetic Patients

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Abstract

The current investigation was designed to seek for the relationship of malondialdehyde (MDA) with the parameters of serum lipid profile in diabetes mellitus. To achieve this purpose, 55 diabetics (11 IDDM patients and 44 NIDDM patients) and 25 age matched healthy subjects were enrolled. It was found that significant (P<0.001) elevations of MDA, S.Tc, S.Tg, LDL-cholesterol and VLDL-triglycerides in both types of diabetics when compared with those of the healthy individuals.The correlation analysis established marked correlation of MDA with S.Tc, STg, and LDL-cholesterol levels in two types of diabetics while VLDL-triglycerides demonstrated obvious correlation with MDA in IDDM.   The result pointed out the interrelation ships of MDA with serum lipid profile in diabetes mellitus.

العلاقة بين فعالية مالون داي الديهايد والتوزيع ألدهني لمرضى السكري

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المستخلص

تم تصميم الدراسة الحالية للبحث عن مركب المالون داي الديهايد والمعايير ألدهنيه ألمصليه في الداء السكري, ولتحقيق هذا الغرض فقد تضمنت الدراسة 55 مريضا بالداء السكري (11 مريضا بالداء السكري من النوع المعتمد على الأنسولين, 44 مريضا بالداء السكري من النوع الغير المعتمد على الأنسولين) وتمت المقارنة مع مجموعة من الأشخاص الأصحاء (25شخص).دلت النتائج على زيادة معنوية ((P<0.001 في مستويات MDA, STc, STg, LDL-cholesterol VLDL-triglycerides لدى مرضى الداء السكري من النوعين عند مقارنتهم مع الأشخاص الأصحاء. بينت النتائج وجود ارتباطات معنوية موجبة بين مستوى MDA ومستويات المعايير الدهون ألمصليه في الداء السكري(S.Tc, S.Tg, LDL-cholesterol) في مرض السكري بنوعيه بينما أظهرت VLDL-triglycerides ارتباطا موجبا مع MDA لدى المصابين بالداء السكري من النوع المعتمد على الأنسولين. تشير هذه النتائج إلى العلاقات الوثيقة بين MDA والدهون المصلية في الداء السكري.

Introduction

The term diabetes mellitus describes a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both[1]. Dyslipidemia is common in diabetes, as both insulin deficiency and insulin resistance affect enzymes and pathways of lipid metabolism[2]. Insulin availability appears to be necessary for normal function of lipoprotein lipase (LPL).Thus, the extreme insulin deficiency associated with severe, uncontrolled diabetes mellitus leads to hypertriglyceridaemia secondary to an acquired LPL deficiency[3]. The lipid pattern in patients with type1 diabetes is largely related to the glycemic control. The Diabetes Control and Complications Trial (DCCT) found that patients with type1 diabetes who were in reasonable glycemic control had similar serum lipid values to normal subjects except for young women, who had somewhat higher serum cholesterol and lower high density lipoprotein (HDL) cholesterol concentration. Controversy, poor glycemic control is associated with hypertriglyceridaemia and in some patients, high serum low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol concentration[4]. Among patients with type2 diabetes, insulin resistance, relative insulin deficiency, and obesity are associated with hypertriglyceridaemia, low serum HDL cholesterol concentration and occasionally high serum LDL cholesterol[5].The ypertriglyceridaemia results from both increased substrate availability (glucose, and free fatty acids) and decreased lipolysis of very low density lipoprotein (VLDL) onset of overt hyperglycemia and is thought to be due in part to hyperinsulinemia[6].

Oxidative stress can be measured by monitoring the changes in blood malonaldehyde. Determination of MDA level is a marker of lipid oxidation. The status of lipid peroxidation in erythrocyte of strptozotocin (STZ) induced diabetic rats by measuring erythrocyte malondialdehyde using a spectrophotometer.The MDA levels were significantly increased in the erythrocytes of strptozotocin induced diabetes rats. This observation indirectly suggests an increase in free radical-mediated damage of the cell [7].

Materials and Methods

Three groups of diabetic patients were enrolled in this study. Group1 consisted of 11IDDM patients. Their ages were 21.20 ± 4.67 year with a range of 15-26 year. Group2 consisted of 44NIDDM patients. Their ages were 50.39 ± 10.98 year with a range of 32-70 year. Diabetic patients were previously diagnosed by physicians. They attended for Emergency Department to Teaching Tikrit Hospital in Tikrit city.

Biochemical Analysis

1- Erythrocyte and Malondialdehyde Assay

Malondialdehyde (MDA) was assayed according to the method of Ohkawa[8] with minor modification. The reactions to form thiobarbituric acid reactive substances (TBARs) depend on the condensation of two molecules of TBA with one molecules of MDA to generate a reddish chromogen that absorb light at 532nm wave length.

2- Determination of serum Cholesterol

The cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinonemine is formed from hydrogen peroxide and 4-aminoantipyrin in the presence of phenol and peroxidase [9].

3- Determination of serum triglycerides

Triglycerides concentration was determined after enzymatic hydrolysis with lipase. The indicator is a quinoneimine formed from hydrogen peroxidase, 4-aminophenazone and 4-chlorophenol under the catalytic influence of peroxidase [10].

4- Determination of serum HDL-cholesterol

LDL and VLDL and chylomicron fractions were precipitated quantitatively by the addition of phosphotungestic acid in the presence of magnesium ions. After centrifugation the cholesterol concentration in HDL fraction which remains in the supernatant was determined [11].

5- Determination of VLDL-c and LDL-c

LDL-c was calculated indirectly by using the friedwald equation [12]:-

LDL-c = Total cholesterol– [VLDL–LDL]

And VLDL-c was calculated:-

VLDL-c = TG/5

Biostatistical analysis

The results were expressed as mean ± SD. Students t-test and linear regression analysis was used for assessment the results of patients and control groups. Significant variation was considered when P value less than 0.05.

Results

1- The measurement of malondialdehyde and serum lipid profile in diabetic patients and healthy individuals

Malondialdehyde (MDA), serum total cholesterol (STC), serum triglycerides (S.Tg), high density lipoprotein-cholesterol (HDL-c), low density lipoprotein-cholesterol (LDL-c), and VLDL-triglycerides, were measured in 55 diabetic patients, and 25 healthy individuals. It was found significant (P<0.001) elevations of MDA, S.TC, S.Tg, LDL-cholesterol, and VLDL- triglycerides levels in both types of diabetics when compared with those of the healthy group. HDL-cholesterol level was demonstrated to be decreased significantly (P<0.001) in the two types of diabetic patients among the same comparison.

2- The correlation of MDA, and serum lipid profile in diabetic patients.

The relationship of MDA with the parameters of serum lipid profile was examined. The data were analyzed by using the linear regression analysis. The results pointed out significant positive correlations of MDA levels with serum cholesterol (r = 0.33,P<0.05 in IDDM and IDDM and r= 0.3, P<0.005 in NIDDM), triglycerides (r = 0.72,P<0.005 in IDDM and IDDM and r= 0.4, P<0.05 in NIDDM), LDL-cholesterol (r = 0.19,P<0.05 in IDDM and IDDM and r= 0.2, P<0.05 in NIDDM), and VLDL-cholesterol (r = 0.7,P<0.005 in IDDM).

Table (1):-Malondialdehyde (nmol/L), and serum lipid profile (Mg/dl), values in diabetic patients and healthy subjects.

	Control N=25	IDDM N=11	NIDDM N=44
MDA	5.04±0.42	10.6±3.92	11.22±2.93
Cholesterol	178± 5.1	267±9.51	319±57.16
Triglycerides	67.01±9.1	215±37.90	295±59.33
HDL-cholesterol	46.00±3.89	24.32±1.90	23.39±4.18
LDL-cholesterol	130±13.70	201±6.54	241±25.02
VLDL-Triglycerides	13.4±5.80	49.23±7.60	53.02±11.9

*:- Differences were significant for all parameters against the control group at a level of $P<0.001$.

Table(1):- Results of univariate analysis of Malondialdehyde (nmol/L), and serum lipid profile (mg/dl), values in diabetic patients.

	IDDM patients		NIDDM patients	
	r	P value	r	P value
Cholesterol	0.33	0.05	0.3	0.05
Triglycerides	0.72	0.005	0.4	0.05
HDL-cholesterol	−0.07	NS	−0.06	NS
LDL-cholesterol	0.19	0.05	0.2	0.05
VLDL-Triglycerides	0.7	0.005	0.11	NS

r = Correlation coefficient. P = Probability

Discussion

The results established marked correlations of MDA contents with serum cholesterol, triglycerides, and LDL-cholesterol levels while HDL-cholesterol didn't show any significant variation. In addition VLDL-triglycerides illustrated only significant correlation with MDA in IDDM. The permanent structural membrane alterations in diabetes and also increased production of reactive oxygen species in the circulation. Further intensification of lipid peroxidation taken place in diabetes mellitus was observed, and this fact may indicate increased production of free radical or diminished efficiency of antioxidant defense mechanism in diabetes compared with healthy subjects [13]. Several studies have reported significant increase in lipid peroxides by thiobarbituric acid substance(TBARS) measurement in diabetes mellitus, however spectrophotometric analysis of TBARS over estimate MAD content, since dialdehydes other than MDA and other plasma component reacts with TBA to form colored complexes, in fact the limited specificity of this method is the main reason for questioning the validity of TBARS in elevating the presence of oxidative stress[14,15,16]. These findings suggested that the

clearance of cholesterol in diabetes mellitus is not related to the glycemic status. The defective VLDL metabolism is essentially dependent on the glycemic control in IDDM, and independent in other diabetics [17]. To verify the details of the biochemical events developing the present data in the enrolled patients, serum cholesterol, triglycerides and LDL-cholesterol are considered as creating factors of hyperlipidaemia in diabetes mellitus. It seems that the activation of lipase is the directing parameters of such abnormality in this disease (18). The defective LDL pathway is also involved, probably through their respecters. Some another believed that serum TG levels are regarded as a better indicator of the vascular disease especially the microangiopathy than serum cholesterol [19,20].

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