EFFECT OF GOOD GLYCEMIC CONTROL ON LIPID PROFILE IN TYPE 2 DIABETES MELLITUS PATIENTS IN AL HUSSEIN TEACHING HOSPITAL

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ABSTRACT:

Background: diabetes markedly increases the incidence of macrovascular complications. For example, the observed 2- to 3-fold greater risk of myocardial infarction with diabetes rises to 8-fold in the presence of hypertension and to nearly 20-fold if both hypertension and dyslipidemia are present; smoking increases these risks even further. As a result, the diagnosis of diabetes mellitus should quickly prompt both an exhaustive search for coexisting cardiovascular risk factors and the initiation of aggressive preventive measures.

Objective: The present study was conducted to evaluate the initial benefit of good glycemic control in patients with type 2 Diabetes Mellitus related dyslipidemia .

Patients and methods: Fasting blood sugar, random blood sugar and lipid profile among 150 patients with type 2 Diabetes Mellitus who were regularly attending diabetes and internal medicine clinic in An Nasiriyah General hospital were measured and observed for the period of the study .

Results: We found that the level of serum cholesterol especially LDL was significantly low in those with good glycemic control in comparison with those with poorly controlled DM . This reduction in serum cholesterol and LDL would be expected to reduce the risk of atherosclerosis and ischemic heart diseases.

INTRODUCTION

Dyslipidemia is a common finding among patients with type 2 Diabetes Mellitus and it is well known that hyperlipidemia increase the risk of coronary artery disease among the diabetic patients . Increased oxidizability of low density lipoprotein is thought to be partly responsible for the diabetes related dyslipidemia. In patients with uncontrolled DM, glycation and oxidative modification of lipoprotein enhance the uptake of these lipids by macrophages initiating the early stages of atherosclerosis . Atherosclerosis involving the coronary, cerebral, and peripheral (lower extremity) arteries is the predominant cause of diabetes-related mortality, responsible for up to 70% of all deaths in patients with this disease. The atherosclerotic process in diabetes is indistinguishable from that of the nondiabetic population, but it begins earlier and is often more extensive and more severe.[1] Diabetes is an *independent* risk factor for accelerated atherosclerosis.

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Its association with vascular disease is not solely attributable to an increased prevalence of other recognized vascular risk factors such as hypertension, smoking, and dyslipidemia. Many abnormalities induced by the diabetic state may contribute to atherosclerosis, including lipid abnormalities (e.g., increased total VLDL and LDL, increased small dense [atherogenic] LDL, decreased HDL, increased lipoprotein oxidation, increased lipoprotein glycosylation, decreased lipoprotein lipase activity), accentuated platelet aggregation and adhesion, endothelial cell dysfunction, and induced procoagulant state (e.g., increased clotting factors and fibrinogen; decreased levels of antithrombin III, protein C, and protein S; and decreased fibrinolytic activity). It has been suggested that hyperinsulinemia per se may contribute to macrovascular disease; proposed pathogenetic mechanisms include insulin-induced stimulation of vascular endothelial and smooth muscle cells, enhanced insulin-like growth factor 1 expression, and augmented synthesis of atherogenic factors such as endothelin and plasminogen activator inhibitor. Moreover, in type 2 diabetes, insulin resistance is an independent risk factor for vascular events and may exert its effect through many of these disease intermediaries. Clearly, the prevention of cardiovascular disease in type 2 diabetes requires a comprehensive and multifactorial approach. Such an approach has been shown to reduce cardiovascular events by almost 50% (Steno-2 study).[2] Dyslipidemia is a crucial therapeutic target in the management of diabetes. The most common lipid disorder associated with diabetes is an increased level of triglyceride-rich lipoproteins (e.g., VLDL), low levels of HDL, and the presence of small dense and, as a result, more

atherogenic LDL particles. The third report of the NCEP Expert Panel continues to identify LDL cholesterol as the primary target for therapy on the basis of overwhelming evidence from clinical trials.[3] This panel has established diabetes as a coronary heart disease "equivalent," meaning that all diabetic patients should strive for LDL levels below 100 mg/dL. In addition, HDL levels should generally exceed 40 mg/dL (50 mg/dL in women); triglyceride levels should fall below 150 mg/dL. Initial steps in treating diabetic dyslipidemia should include optimization of glycemic control, dietary reinforcement, and a prescription of aerobic exercise.[4] The present study was carried out to evaluate the initial benefit of glycemic control in patients with type 2 Diabetes Mellitus on the occurrence and progression of dyslipidemia and to correlate between the glycemic indices and serum lipid profile.

METHODS & MATERIAL

The study was conducted on clinical data of patients with known type 2 Diabetes Mellitus who were regularly attended internal medicine and diabetes clinic in An Nasiriyah General hospital-Thi Qar ,Iraq. The fasting blood samples of the patients were analysed in the clinical laboratory of the hospital and the patients clinical data were entered in the recorded book of the laboratory for a period from April 2006 to November 2007 .clinical data of 150 patients with normal liver function and renal function were randomly selected for the study, depending on their mean fasting blood sugar, the patients were classified into three groups:

Group A : consist of 41 (12 male 29 female) patients regarded to have good

glycemic control with mean fasting blood sugar of less than 130 mg/dl

Group B : consist of 52 (22 male 30 female) patients regarded to have satisfactory glycemic control with mean fasting blood sugar ranging from 131 – 160 mg/dl.

Group C : consist of 57 (24 male 33 female) patients regarded to have poor glycemic control with mean fasting blood sugar of more than 160 mg/dl.

The patients had not taken insulin or other medications for a minimum 10 hours prior to the blood sample collection.

BIOCHEMICAL ASSAY

Samples for fasting blood sugar, random blood sugar, blood urea, serum creatinine, ALT, AST,total serum cholesterol ,HDL,LDL and TG were analysed by automatical spectrophotometer using commercial kit supplied by Roche company. The very low density lipoprotein (VLDL) was calculated by substruction of LDL-cholesterol +HDL- cholesterol from the total cholesterol and the ratio of HDL-cholesterol/ total cholesterol was calculated by dividing the two means of each group. The mean of fasting blood sugar of each group was calculated.

STATISTICAL ANALYSIS

The presented data are mean ±SD. The significance of differences between the means was computed by one way analysis of variance followed by multiple comparison analysis. Spearman 's regression analysis was used to study the significance of correlation between serum glucose (as an independent parameter) and the individual serum lipid (as dependent parameter). P value less than 0.05 was consider significant.

RESULTS

The good glycemic control group had fasting glucose level less than 130 mg/dl. and random blood glucose (mean) less than 200 mg/dl. with mean values of 121.02±8.56mg/dl. and 162.6±26.23 mg/dl. respectively. The satisfactory glycemic control group had fasting blood glucose range from 131-160 mg/dl. with mean value of 142.31±11.03 mg/dl. and random blood glucose (mean) range from 200-250 mg/dl. with mean values of 223.42±14.08. The poorly glycemic control group had fasting glucose level more than 160 mg/dl. and random blood glucose (mean) more than 250 mg/dl. with mean values of 228±36.7 mg/dl. and 282 ± 41.36 mg/dl. respectively. A strong correlation was coexist between blood glucose level and lipid profile. The serum total cholesterol in the satisfactory glycemic control group shows a trend of increase by 6.8% compared with the good glycemic control group but this increase is not statistically significant .However in the poor glycemic control group ,the serum total cholesterol was significantly increased by 21.3% compared to good glycemic control group. Serum triglyceride also exhibited a significant (p value < 0.001) increase in the poor glycemic control group which amounted to be 66.3% compared to the good glycemic control group and by 31.8% compared to the satisfactory glycemic control group. The VLDL cholesterol was raised in the poor glycemic control group by 36.4% (p value<0.005) compared to the good glycemic control group and by 24.2 % (not statistically significant) compared to the satisfactory glycemic control group. Similarly, the LDL cholesterol was significantly(p value < 0.01) increased by 21.1% in the satisfactory glycemic

control group and by 32 %(p value < 0.001) in the poor glycemic control group compared to good glycemic control group. In contrast the HDL cholesterol in the satisfactory glycemic control group reveal a significant reduction (P value < 0.05) and a 22% reduction in the poor glycemic control group compared to good glycemic control group

DISCUSSION

Diabetes mellitus regarded as risk equivalent for cardiovascular diseases .metabolic changes occur in diabetes mellitus considered to be one of the major risk factors for coronary artery diseases. While patients with type 2 were not studied in the DCCT, the eye, kidney, and nerve abnormalities are quite similar in both types of diabetes, and it is likely that similar underlying mechanisms apply. Several important differences, however, must be considered. Since type 2 patients are generally an older population with a high incidence of macrovascular disease, Moreover, Weight gain may be much greater in obese type 2 patients in whom intensive insulin therapy is attempted. The risks take on greater relevance in older type 2 patients, who have relatively lower prevalence of microangiopathy than type 1 patients and in whom prevention of microvascular disease over the long term is much less likely to influence morbidity and mortality because of greater consequences of their macrovascular disease. [5] The Kumamoto study was shown that intensive insulin therapy significantly reduced microvascular end points. The data from the UKPDS and this study provide support for guidelines recommending vigorous

treatment of concomitant microvascular and cardiovascular risk factors in patients with type 2 diabetes. [6] In our patients none was found to have LDL – cholesterol meeting the recommended level ((< 2.6 mmol/ L.)) even in those with good glycemic control group while TG were as per recommendations in those with good glycemic control group but not in the others. HDL – cholesterol was meeting the recommendation level in most of our patient. Many epidemiological studies has pointed to the importance of raised plasma TG and low HDL – cholesterol as a risk for coronary disease in diabetic patients [7,8] and there is supportive evidence for aggressive management of lipid disorders in type 2 diabetes[9,10,11,12]. Majority of our patients have hypertriglyceridaemia and high LDL – Cholesterol level particularly those in the satisfactory and poor glycemic control groups which is consistent with other studies [7,8,9,10,11,13]. However no significant changes in the level of HDL – cholesterol compared with other studies [7,14],Which, is also a modifiable risk factor for coronary vascular disease. Although evidence has been provided for new treatment guidelines regarding dyslipidaemia in diabetes[15,16], However to apply these guidelines to our patients we need more controlled studies. As far as glycaemic status and lipid disorders are concerned, Hypertriglyceridemia was observed more significantly in the poorly controlled group with statically quite significant result but it needs to be evaluated on a larger scale as there are studies showing that improved control of hyperglycaemia do modify diabetes associated dyslipidaemia[7,17]

TABLES

Table 1 : fasting and random blood glucose in different glycemic control groups *

Parameter	good glycemic control (n.41)	satisfactory glycemic control (n. 52)	poor glycemic control (n. 57)
fasting blood glucose mg/dl.	121.02±8.56	142.31±11.03	228±36.7
random blood glucose mg/dl.	162.6±26.23	223.42±14.08	282 ± 41.36

*presented data are mean ±SD p value < 0.05

Table 2 :Lipid profile in type 2 **Diabetes Mellitus ***

parameter	good glycemic control (n.41)	satisfactory glycemic control (n. 52)	poor glycemic control (n. 57)
Serum cholesterol mmol/l.	5.22 ± 1.08	5.62 ± 0.91	6.21 ± 1.58
Serum TG mmol/l.	1.35± 0.29	1.6 ± 0.36	2.14 ± 0.81
HDL mmol/l.	1.36 ± 0.48	1.12 ± 0.19	1.06 ± 0.18
VLDL mmol/l.	0.74± 0.26	0.88 ± 0.28	1.09 ± 0.38
LDL mmol/l.	3.08±0.53	3.64 ± 0.56	4.08±0.62

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*presented data are mean ±SD p value < 0.05

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