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SERUM LIPIDS, LIPOPROTEINS AND URIC ACID IN TYPE II DIABETES MELLITUS ON SULPHONYLUREA AND INSULIN MEDICATIONS

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ABSTRACT

One hundred and forty five, non-insulin dependent-diabetes Mellitus (NIDDM), without ischemic heart disease, one hundred and twenty three, NIDDM, with ischemic heart disease patients and eighty-seven healthy subjects were selected in this study. NIDDM patients (group III) showed highly significant increase of total LDL, VLDL cholesterol, triglycerides and uric acid with low levels of HDL-c compared to NIDDM (group II) and healthy subjects (group I). Except for uric acid and HDL-c, all parameters of NIDDM group showed high concentrations compared to healthy subjects. The NIDDM group without ischemic heart disease showed a significantly increase for triglycerides (TG and VLDL-c but no significant increase was noticed for uric acid (UA) on oral medication of hypoglycemic agent (sulphonylurea) compared to the medication of insulin.

The NIDDM patients with ischemic heart disease showed a higher results for total cholesterol (TC), LDL-c, VLDL-c, TG and a lower result for HDL-c upon medication of oral hypoglycemic agent (sulphonylurea) compared to medication on insulin.

INTRODUCTION

There were lipid abnormalities in diabetes, the most common lipid abnormalities in diabetes is raised TG levels due to excess of V-LDL-c concentration (Pickup and Willm 1994). HDL-c levels are reduced in NIDDM, in proportion to increased TG and VLDL-c, and thus associated with increased risk of premature ischemic heart disease and increased mortality and morbidity in patients with coronary heart disease (Martial and Bourassa 1995). Kennedy *et al.* (1978) found that HDL-c concentrations were shown to be lower in NIDDM than in those with insulin dependent-diabetes (IDDM) and control.

Commencement of theory with either insulin or oral sulfonylureas leads to a reduction in VLDL-c levels and an increase in HDL-c, despite the weight gain that often accompanies the initiation of therapy in NIDDM patients (Rabkin *et al.* 1983 and Abate and Brunzell 1990).

The actual mechanisms by which HDL-c levels are determined are not known, but a current hypothesis is that HDL-c reflects the rate of catabolism of TG and VLDL-c (Tall *et al.* 1978). On entering plasma, chylomicrons and VLDL-c become a substrate for the endothelial bound

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enzyme, lipoprotein lipase, this enzyme, which requires insulin for its synthesis and hydrolysis triglycerides from the core of the lipoproteins. As the particles is successively delipidated apoproteins and lipids on its surface are believed to form nascent HDL particle. Thus, situation in which chylomicrones or VLDL flux is impaired would lead to low levels of nascent HDL. Laakso *et al.* (1986) showed an association between low levels of HDL-c and coronary heart disease (CHO) in both NIDDM and IDDM.

The aim of this work is to throw some light on the effect of diabetes mellitus type II and ischemic heart disease on serum lipids, lipoproteins and uric acid.

MATERIALS AND METHODS

Subjects

The subjects were divided into three groups: Group-I: controls, eighty-seven subjects (45 males and 42 females) with mean ages 57.1± 9.89 years were selected randomly. They were non-smokers, non-alcoholics, no family history of coronary heart disease (CHD), not obese and not diabetics or hypertension. Group-II: one hundred and forty-five adults (66 males and 79 females), non-insulin dependent, diabetes Mellitus (NIDDM group) with mean ages 58 ± 10.46 years were selected randomly at the diabetic clinic during their routine visits from Sede-Ehsain polyclinic. Patients were not on medication except for the antidiabetic therapy oral hypoglycemic agent (sulphonylurea) or insulin. Group-III: diabetic patients; one hundred and twenty-three adults (45 males and 78 females) with mean ages 59.32 ± 9.83 years who were apparently suffering from ischemic heart disease as judged from their medical history were selected at randomly from Sede-Ehsain Polyclinic, 7th October Hospital, and El-Jamaheria Hospital, Benghazi, Libya, during the period from 1st May 2002 to 1st March 2003. All patients received antidiabetic therapy and didn't take lipid lowering medication. The patients were diagnosed as myocardial infarction and angina pectoris, at the time of blood sampling. None of patients had acute myocardial infarction within 3 months.

Sampling

Five ml of venous blood samples were collected after fasting overnight at least 10 hr. The samples were kept for 30 minutes at room temperature, then serum was separated by centrifugation at 4,000 r.p.m. for 15 minutes. The serum stored at about - 18°C until analysis.

Methods

Triglycerides were determined by means of kits obtained from Biocon Company, Germany according to the method of Fassati and Prenciple (1982). Total cholesterol was determined according to Richmond (1973), HDL-c was determined according to Lopes *et al.* (1977). LDL-c was determined according to the method of Levy (1981) and uric acid was determined according to Pileggi and Barthelmai (1962). VLDL-c was calculated from the following equation according to Bugrin *et al.* (2005):

$$VLDL\text{-}c = [Total\ Cholesterol] - [LDL\text{-}c + HDL\text{-}c]\ mg/dl$$

Statistical Analysis

The recorded data in this study were subjected to statistical analysis according to Schaumn's (1992).

RESULTS

Serum lipids, lipoproteins and uric acid of healthy subjects (control-group I), NIDDM group without ischemic heart disease (group II) and NIDDM patients suffering from ischemic heart disease (group III) (Table 1). The mean levels of serum total-c, triglyceride and VLDL-c in all NIDDM group in spite of with or without ischemic heart disease were significantly higher than in healthy group, while a significant decrease in HDL-c were observed. The difference in uric acid was not significant in NIDDM and healthy groups.

The mean levels serum total-cholesterol, triglycerides and uric acid in NIDDM patient were significantly increase than that observed in NIDDM and healthy groups, while a significant decrease in HDL-c were found.

Data in Table 2 represent the serum cholesterol, TG, HDL, LDL, VLDL and uric acid in NIDDM (group II) without ischemic heart disease, oral hypoglycemic agent (sulphonylurea) and insulin treated. The mean serum levels of triglycerides, VLDL-c and uric acid in NIDDM group on medication of oral hypoglycemic agent (sulphonylurea) were higher than that observed in NIDDM group on medication of insulin. The difference in means serum levels of total-c and LDL-c were not significant.

Table 1. Serum lipids, lipoproteins and uric acid concentration in healthy group, NIDDM group and NIDDM patient.

Groups	N	CHOL	TG	HDL	LDL	VLDL	UA
I Healthy group	87	163.79 ± 28.48	120.85 ± 38.55	43.66 ± 8.11	94.82 ± 25.89	24.45 ± 8.52	3.92 ± 0.86
II NIDDM group	145	184.68 ± 31.13	186.37 ± 96.46	36.79 ± 6.01	111.89 ± 27.47	36.96 ± 18.99	3.88 ± 0.80
	P	0.001	0.00	0.00	0.00	0.00	0.36
III NIDDM Patients	123	211.38 ± 46.5	235.1 ± 156.65	32.34 ± 6.28	139.25 ± 40.79	46.66 ± 30.66	6.10 ± 1.39
	P'	> 0.001	> 0.01	> 0.001	> 0.001	> 0.009	> 0.001
	P''	> 0.001	> 0.001	> 0.001	> 0.001	> 0.001	> 0.001

n: number of patients

p: *p* values of NIDDM group vs. control

p': *p* values of NIDDM group vs. NIDDM patients, *p*'': *p* values of NIDDM patients vs. control

Table 2. Serum lipids, lipoproteins and uric acid in NIDDM group oral hypoglycemic agent (sulphonylurea) and insulin treated as mg/dl mean ± SD.

NIDDM Groups	CHOL	TG	HDL	LDL	VLDL	UA
(A) Oral treated	184.59 ± 30.18	200.9 ± 108.52	36.63 ± 6.03	110.51 ± 27.89	39.02 ± 21.37	3.98 ± 0.78
(B) Insulin treated	185.1 ± 32.77	170.12 ± 72.72	37.48 ± 6.00	113.97 ± 26.94	33.86 ± 14.37	3.70 ± 0.82
P	0.45	0.03	0.20	0.23	0.05	0.02

Data in Table 3 show the serum total cholesterol, TG, HDL, LDL, VLDL and uric acid in NIDDM patients with ischemic heart diseases oral hypoglycemic agent (sulphonylurea) and insulin treated.

Table 3: Serum lipids, lipoproteins and uric acid in NIDDM patients with ischemic heart diseases oral hypoglycemic agent (sulphonylurea) and insulin treated as mg/dl mean ± SD

NIDDM Patients	CHOL	TG	HDL	LDL	VLDL	UA
(A) Oral treated	213.74 ± 45.93	257.38 ± 177.96	31.87 ± 6.50	141.71 ± 42.00	51.48 ± 31.55	6.10 ± 1.27
(B) Insulin treated	207.29 ± 47.73	201.51 ± 102.6	33.16 ± 5.85	135.0 ± 38.62	40.3 ± 29.36	6.10 ± 1.60
P	0.23	0.03	0.14	0.40	0.03	0.50

The means serum levels of triglycerides and VLDL-c in NIDDM patients on medication of oral hypoglycemic agent were significantly higher than that observed in NIDDM patients on medication of insulin. While the difference in means levels of total, LDL and HDL cholesterols and uric acid were not significant.

DISCUSSION

The high plasma triglycerides and low HDL values in NIDDM is consistent with reported decrease lipoprotein lipase activity and with impaired catabolism of TG-rich lipoprotein in type II diabetics (Nikkila 1981 and Brunzell *et al.* 1979). As lipoprotein lipase required insulin for its synthesis and hydrolysis of TG-from the core of the lipoproteins, type II diabetes whose hyperglycemia dose not respond to a diabetic diet and oral medication can be treated with insulin (Rosenzweig 1994). Also, the major effect of the sulphonylureas oral hypoglycemic compound is the lowering of the blood sugar level by stimulation of production or release of insulin from the beta-cells of the pancreas (Harlod 1994).

This study showed that a significant difference in serum levels TG and VLDL-c between NIDDM group and NIDDM patients on medication of oral hypoglycemic agent (sulphonylurea) and medication of insulin. But there was no difference between total cholesterol and LDL-c values in the two groups. The increased level of TG and VLDL-c in oral hypoglycemic agent is consistent with hypothesis which was suggested that the level of TG and VLDL-c are related to impairment in TG rich

lipoprotein catabolism. The only other attribute postulated to explain HDL-c differences in diabetics, sulphonylurea therapy, did not contribute to HDL-c differences I diabetics in this population (Nikkila 1981 and Brunzell *et al.* 1979). In contrast to previous reports of lower levels of HDL-c in sulphonylurea treated diabetics (Kennedy *et al.* 1978 and Stanton 1978). In this study, there was no significant difference in HDL-c level in patients on sulphonylurea hypoglycemic agents vs. those on insulin treatment alone. These findings are in consistent with study by Hopkins (1983). Furthermore, a statistical significant incidence of hyperuricemia in group of diabetic patient with CHD has been evident in our study. Also, we found the difference in uric acid levels in diabetic with oral hypoglycemic agent were significantly higher than diabetics on medication of insulin. These differences for the two treatment diabetics with CHD was not detected.

REFERENCES

Abbate, S. K. and Brunzell, J. D. (1990): Pathophysiology of hyperlipidemia in diabetes mellitus. J. Cardiovase Pharmacol., 16:51.

Brunzell, J. D., Porte, D. J. and Bierman, E. L. (1979): Abnormal lipoprotein lipase mediated plasma triglyceride removal in untreated diabetes mellitus associated with hypertriglyceridemia. Metabolism, 28: 897.

Bugrin, S. N., Issa, I. G. and Alberghothy, A. A. (2005): Comparison study of serum lipids, lipoproteins and uric acid for male and female in diabetic patients with ischemic heart disease. Sci., J. Fac., Sci., Minufiya Univ., 125.

Fassata, P. and Prenciple, L. (1982): Serum triglycerides determined colorimetrically with an 196-enzyme that produces hydrogen peroxide. Clin Chem., 28: 2007.

Harold, E. L. (1994): Oral antidiabetic agents. In: Jeslin's Diabetes Mellitus, 13th ed.

Hopkins, J. (1983): A community study of HDL in adult NIDDM. Am. J. Epidemial., 117: 186.

Kennedy, A. L.; Lappin, T. R.; Lavery, T. D. and Hadden, D. R. (1978): Relation of high density lipoprotein cholesterol concentration to type of diabetes and its control. Br. Med. J., 23: 1191.

Laakso, M.; Pyorala, K. and Sarlund, H. (1986): Lipid and lipoprotein abnormalities associated with coronary heart disease in patients with insulin-dependent diabetes mellitus. Atheroselekosis 6: 679.

Levy, R. R. (1981): Cholesterol, lipoprotein, apolipoprotein and heart disease. Recent status and future prospects. Clin. Chem., 27: 653.

Lopez, M. F.; Stone P.; Ellis S. and Collwell J. A. (1977): Cholesterol determination in high density lipoproteins separated by three different methods. Clin. Chem. 23 (5): 882-886.

Martial, G. and Bourassa, M. D. (1995): Therapeutic approach in patients with diabetes and coronary artery disease. www.fac.org.ar/SCVC/llave/pdf/bourassi.pdf.

Nikkila, E. A. (1981): High density lipoproteins in diabetes. Diabetes, 30: 82.

Pickup, J. and William, G. (1994): A Textbook of Diabetes (1st edition, vol. 2), Blackwell-Scientific Publication.

Pileggi, R. and Barthelmai, W. (1962): Klin. Wochemschr, 40: 585-589.

Rabkin, S. W.; Boyko, E. and Streja, D. A. (1983): Changes in high density lipoprotein cholesterol after intiation of insulin therapy in non-insulin diabetes mellitus: Relationship to changes in body weight. Am. J. Med. Sci., 14: 285.

Richmond, W. (1973): Preparation and properties of cholesterol oxidase from Nocardia sp. and its application to enzymatic assay of total cholesterol in serum. Clin. Chem., 19: 1350.

Rosenzweig, J. L. (1994): Principle of insulin therapy. In: Joslin's Diabetes Mellitus (13th ed.).

Schaumn, S. (1992): Theory and problems of statistics. In: Schaumn's Outline Series, second edition.

Stanton, K. (1978): HDL-cholesterol in diabetes and heart disease. Lancet, 2: 638.

Tall, B. R. and Small, D. M. (1978): Plasma high density lipoprteins. Engl. J. Med., 299: 1232.

تأثير مرض السكرى من النوع II على الدهون والكوليسترول وحامض اللبوريك في مرضى القلب

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في هذه الدراسة تم أخذ ثلاثة مجموعات هي : 1) المجموعة الأولى : وتتكون من 87 شخص من الأصحاء غير المصابين بمرض السكرى وأرتفاع ضغط الدم ، 2) المجموعة الثانية : وتتكون من 145 شخص وكان التشخيص الأكلينيكي لهم هو إصابتهم بمرض داء السكرى الغير معتمد على الأنسولين ، 3) المجموعة الثالثة : وتتكون من 123 شخص وكان التشخيص الاكلينيكي لهم هو إصابتهم بمرض الشرايين التاجية وداء السكرى الغير معتمد على الأنسولين.

وقد تم تقسيم المرضي التابعين للمجموعتين الثانية والثالثة إلي تحت مجموعتين هما : 1) المجموعة الأولي وفيها يعالج المرضي بواسطة الكبسولات مخفضات السكر والتى يتم تناولها عن طريق الفم ، 2) والمجموعة الثانية: ويخضع المرضى التابعين لها للعلاج بواسطة الأنسولين ، عن طريق الحقن . وبمقارنة النتائج المتحصل عليها بهاتين المجموعتين وجد أن متوسط معدلات الكوليستيرول ، TG. VLDL. LDL. تكون مرتفعة في المجموعة الأولى التي عولجت بالكبسولات مقارنة بالمجموعة الثانية التي عولجت بواسطة الأنسولين . ولم يلاحظ فروق معنوية بين متوسط معدلات حامض اليوريك في كلا المجموعتين .