ORIGINAL ARTICLE

Postprandial lipemia in diabetic men during hypolipemic therapy

Anna Skoczyńska, Bogusława Kreczyńska, Rafał Poręba

Department of Internal Medicine, Occupational Diseases and Hypertension, Wrocław Medical University, Wrocław, Poland

KEY WORDS

hyperlipemia, postprandial lipemia, type 2 diabetes mellitus

ABSTRACT

INTRODUCTION Mechanisms underlying postprandial lipemia in various pathological states remain to be elucidated.

OBJECTIVES The aim of the study was to evaluate lipid homeostasis in men with type 2 diabetes mellitus (DM) after a standard meal. Moreover, the effect of short-term hypolipemic therapy on postprandial lipemia was assessed.

PATIENTS AND METHODS Twenty-six men with DM aged 53 ±6.7 years, 27 patients with hyperlipemia and no DM (asymptomatic hyperlipemia – AH) and 60 normolipemic subjects aged 46 ±11 years were included in the study. Treatment with simvastatin (20 mg/d) or fenofibrate (267 mg/d) was initiated in all DM patients due to fasting hyperlipemia, and in the AH group. Blood samples were drawn in the fasting state and 3 h after a meal at three time points, i.e. at baseline, after 6 and 12 weeks of treatment. Triglycerides (TG), glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), HDL_2-C, and HDL_3-C were assayed by routine laboratory tests; apolipoproteins A and B by immunoturbidimetry, and high-sensitivity C-reactive protein (hsCRP) by immunonephelometry.

RESULTS In men with DM, changes in triglycerides induced by a meal (140 ±68.0 mg/dl) were higher compared to normolipemic men (62.1 ±52.5 mg/dl, $p < 0.001$) or AH subjects (76.3 ±80 mg/dl, $p < 0.05$). There were no linear correlations between the levels of TG (or HDL cholesterol) and HDL_3-C, or between TG and hsCRP in the DM group. Hypolipemic treatment decreased fasting lipid and hsCRP levels, significantly reduced postprandial lipemia ($p < 0.001$) and restored some correlations between lipid variables observed in the control group, but not those with hsCRP.

CONCLUSIONS Type 2 DM is associated with increased postprandial lipemia and abnormal lipid homeostasis. Lipid intolerance detected in a postprandial lipemia test may be an indication for hypolipemic therapy.

Correspondence to:
Prof. Anna Skoczyńska, MD, PhD, Katedra i Klinika Chorób Wewnętrznych, Zawodowych i Nadciśnienia Tętniczego, Akademia Medyczna, ul. Pasteura 4, 50-367 Wrocław, Poland, phone: +48-717-84-25-22, fax: +48-713-27-09-54, e-mail: annaskoc@ak.am.wroc.pl
Received: April 9, 2009.
Revision accepted: June 2, 2009.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2009; 119 (7-8): 461-468
Tłumaczyła Małgorzata Kolcz, MD

INTRODUCTION Lipid metabolism induced by a meal has a greater influence on the circulatory system than the fasting lipid profile because the postprandial phase lasts longer than the fasting phase in modern lifetime. Postprandial lipemia is characterized by increased levels of exogenous triglycerides (TG) present in chylomicrones (CM), and endogenous TG in very low-density lipoproteins (VLDL), which are synthesized in the liver. Postprandial hypertriglyceridemia results from the competition between CM and VLDL for lipoprotein lipase (LPL) and hepatic receptors. LPL hydrolyzes TG contained in CM and VLDL, which contributes to the production of smaller remnant atherogenic lipoproteins (remnants).[1-3] The transport of TG from VLDL and cholesterol into VLDL particles is enhanced. As a result of these processes, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) particles become abundant in TG, small and dense LDL are produced, and HDL are metabolized in the liver and kidneys at a higher rate.[4]

Hypertriglyceridemia is considered as an independent cardiovascular risk factor.[5] In atherogenic

dyslipidemia it coexists with HDL deficiency, which additionally increases morbidity and mortality rates.[6] High postprandial lipemia, or postprandial dysregulation of metabolism, is another risk factor inducing oxidative stress, which increases the postprandial rise in glucose and TG levels. These anomalies are observed in poorly controlled diabetes, abdominal obesity, and insulin resistance.[1,2] Hypolipemic therapy in a high risk population, including patients with coronary artery disease, restores normal lipid profile and reduces postprandial lipemia.[7]

Postprandial lipemia is usually evaluated as changes of the area under the curve of triglyceridemia, assessed at consecutive hours after a standard meal. Relevant data can also be obtained from the analysis of absolute and relative lipid changes (compared to the fasting value) evaluated at a particular point of time, preferably when changes in TG levels are most pronounced, e.g. 3 h after the meal. The mechanisms of lipid homeostasis after stimulation remain to be elucidated. Associations between maximum fasting and postprandial lipemia values or postprandial changes in inflammatory activity remain unclear.

The aim of the study was to compare lipid and protein alterations induced by a high-fat meal in men with diabetes mellitus (DM) and subjects with normal lipid profile. Since all patients with DM had lipid abnormalities, the second control group comprised men with hyperlipemia and no DM. In addition, the effect of short-term hypolipemic therapy on postprandial lipemia and potential postprandial changes in inflammatory response were investigated.

PATIENTS AND METHODS

Study groups Postprandial lipemia was induced by a standard meal in 113 men: 26 with type 2 DM, 27 with hyperlipemia and no DM (asyptomatic hyperlipemia – AH), and 60 normolipemic subjects. Exclusion criteria were as follows: liver, kidney and thyroid diseases, inflammatory disorders, and malignancy. In the DM group 14 men had hypercholesterolemia (defined by the National Cholesterol Education Program [NCEP] as fasting cholesterol >200 mg/dl) and 12 patients had hypertriglyceridemia (defined by the NCEP as fasting TG >200 mg/dl). In the AH group 17 patients had hypercholesterolemia and 10 men had hypertriglyceridemia. Subjects with DM received oral hypoglycemic drugs and no insulin. The characteristics of the study groups are presented in TABLE 1.

According to the guidelines of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes[8], patients with DM and hypercholesterolemia received statin as a first choice drug (class Ia indication), patients with DM and hypertriglyceridemia received fibrate (Lipanthyl, Solvay) (class IIb indication). Simvastatin (Simvasterol, Polpharma) was administered in a daily dose of 20 mg and fenofibrate in a dose of 267 mg/d. The same therapy was administered in men with hyperlipemia and no DM. No side effects were observed.

All men underwent physical examination. Blood samples were obtained from each participant at baseline, after 6 and after 12 weeks of therapy. In the control group blood samples were drawn once in the fasting state and after a meal.

Blood samples were obtained 12 h after the last meal and 3 h after eating a standard high-fat meal (100 g of fat, 1500 kcal). The fat composition determined by gas chromatography was as follows: 41.4% – oleinic acid, 24.7% – palmitic acid, 16.7% – stearic acid, 8.8% – linoleic acid and 9.4% – other acids.

All patients gave their informed written consent. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee in Wrocław.

Biochemical parameters Total cholesterol, HDL cholesterol (HDL-C) and TG were assayed with the SPINREACT kit (Sant Esteve De Bas, Girona, Spain). LDL cholesterol (LDL-C) levels were measured using Friedewald equation. The QUANTOLIP® HDL kit (Technoclone GmbH, Vienna, Austria) was used for precipitation of cholesterol into HDL2 and HDL3 cholesterol subfractions (HDL2-C and HDL3-C).

TABLE 1 Demographic and clinical characteristics of the study groups: with type 2 diabetes mellitus (DM), hyperlipemia and no DM (asymptomatic hyperlipemia – AH) and controls. Data are given as mean ± standard deviation, unless otherwise stated.

Variables	DM (n = 26)	AH (n = 27)	Control (n = 60)
age (years)	53.1 ±6.7	46.0 ±11.0	45.6 ±11.2
body mass index (kg/m^2)	33.6 ±6.5[a]	27.6 ±3.0	28.9 ±5.2
current smokers, n (%)	10 (38%)	13 (48%)	18 (30%)
hypertriglyceridemia, n (%)	12 (46%)	10 (37%)	0 (0%)
hypercholesterolemia, n (%)	14 (54%)	17 (63%)	0 (0%)
triglycerides (mg/dl)	254 ±137[a]	267 ±150[a]	132 ±49
total cholesterol (mg/dl)	219 ±37.0	219 ±38.0	174 ±28.8
low-density lipoprotein cholesterol (mg/dl)	124 ±41.8	121 ±31.8	110 ±36.6
high-density lipoprotein cholesterol (mg/dl)	41.0 ±11.4	45.2 ±11.3	44.4 ±8.5

a significant difference between mean values in the study and control groups at $p < 0.001$

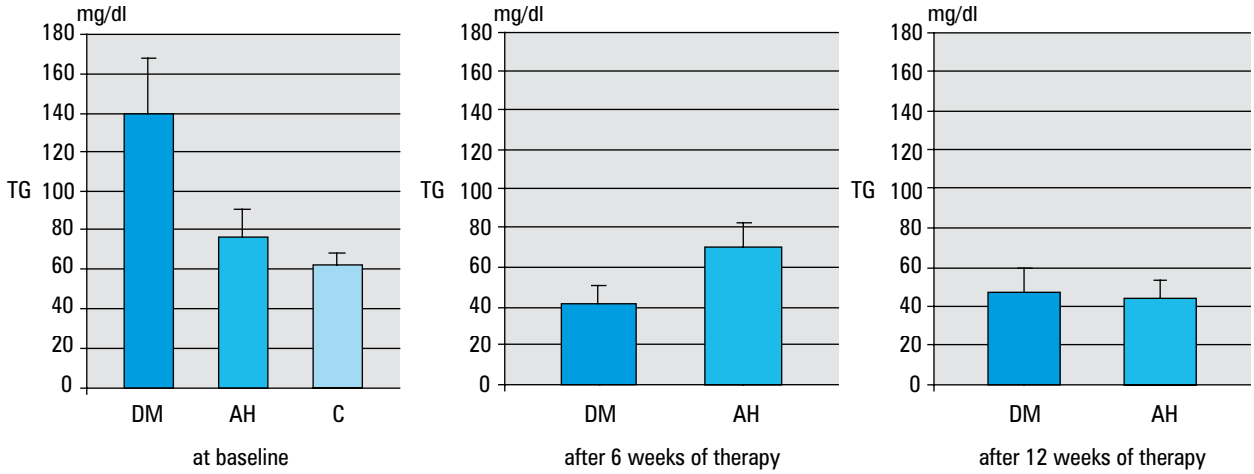

FIGURE Changes in plasma triglyceride levels (ΔTG) in men with type 2 diabetes (DM, n = 26), patients with hyperlipemia and no DM (asymptomatic hyperlipemia – AH, n = 27) at baseline, after 6 and 12 weeks of hypolipemic therapy, and the control group (C, n = 60). Data are given as mean ± standard error of mean.

Levels of apolipoproteins A and B (apo A and B) were determined by immunoturbidimetry with the DADE Behring Marburg GmbH test (Marburg, Germany). High-sensitivity C-reactive protein (hsCRP) levels were measured by immunonephelometry using the CardioPhase hsCRP Dade Behring kit. The results are evaluated by comparison with a standard concentration in N Rheumatology Standard SL against the international reference preparation BCR – CRM 470.

Statistical analysis Statistical analysis was performed using Statistica PL 6.0 software (Stat Soft, Poland). Mean value and standard deviation (SD) of variables were estimated (the standard error of the mean [SEM] value is presented in the FIGURE). The Shapiro-Wilk test was used to assess the distribution of variables. In the case of variables with non-normal distribution the Kruskal-Wallis one-way analysis of variance (ANOVA) was used. Differences between mean value of variables were assessed with the post-hoc Newman-Keuls test. Correlations between the study parameters were expressed as correlation coefficient (r) – Pearson's for variables with normal distribution or Spearman's for variables with non-normal distribution. A $p < 0.05$ was considered statistically significant.

RESULTS

Changes in lipid metabolism and inflammatory activity in patients with type 2 diabetes In patients with DM absolute postprandial increase in TG levels (postprandial TG value minus fasting TG value, $\Delta TG = TG_p - TG_o$) before the therapy (140 ±68.0 mg/dl) was significantly higher compared to men with hyperlipemia and no DM (76.3 ±80 mg/dl, $p < 0.05$) or to normolipemic controls (62.1 ±52.5 mg/dl, $p < 0.001$).

Statistically significant changes in lipid and glucose levels occurred during the hypolipemic therapy (TABLE 2). Statin administration led to a decrease in total cholesterol and LDL levels (after 12 weeks of therapy: 233 ±28 mg/dl to 187 ±37 mg/dl, 143 ±47 mg/dl to 107 ±34 mg/dl, respectively). A 12-week fibrate therapy reduced TG levels (from 280 ±95.8 mg/dl to 224 ±104 mg/dl) and increased HDL-C levels (from 39.0 ±9.1 mg/dl to 45.6 ±10.9 mg/dl).

Hypolipemic therapy reduced postprandial lipemia induced by a high-fat meal in patients with DM. There was a significantly lower increase in postprandial TG levels already after 6 weeks of treatment ($p < 0.001$). The reduction in lipemia was maintained until the 12th week of the therapy (FIGURE). Fibrate was more effective (ΔTG reduced from 126 ±115 mg/dl to 33 ±56 mg/dl, n = 12, $p < 0.05$) than statin (ΔTG reduced from 107.8 ±84 mg/dl to 36 ±61 mg/dl, n = 14, $p < 0.01$).

Changes in lipid metabolism and inflammatory activity in patients with hyperlipemia and no diabetes After 6 weeks of hypolipemic treatment, mean fasting LDL-C levels were decreased ($p < 0.05$) but the effect was not observed after 12 weeks of the therapy. TG and HDL-C levels did not change significantly. Medications administered during the study did not have a significant effect on glucose, apo A, apo B, and hsCRP levels (TABLE 3).

Prior to treatment, postprandial lipemia (ΔTG) in patients with AH (76.3 ±80 mg/dl) was insignificantly higher compared to the control group (62.1 ±52.5 mg/dl). Statin or fibrate administration did not have any effect on lipemia induced by a high-fat meal until the 12th week of treatment (FIGURE).

The reduction in postprandial changes in TG, induced by hypolipemic drugs, was similar in the statin (reduction from 68.3 ±81.6 mg/dl to 42.5 ±35.6 mg/dl, n = 17) and the fibrate groups (reduced from 71.9 ±59.3 mg/dl to 54.6 ±63.2 mg/dl, n = 10).

Correlations between lipid and protein parameters during hypolipemic therapy in the study groups In all men positive linear correlations between fasting apo B and LDL-C levels (r = 0.37, $p < 0.001$), and between apo A and HDL-C levels (r = 0.49, $p < 0.001$) were detected. These associations were observed both in the fasting state and after the meal in separate groups (TABLE 4).

A positive correlation between TG and apo B levels in the fasting state and/or postprandially was noted after 6 weeks of hypolipemic therapy in DM patients, and 12 weeks of treatment in AH

TABLE 2 Fasting and postprandial levels of lipids, glucose, C-reactive protein, apolipoprotein A and B measured in 26 diabetic men before and during hypolipemic therapy

	Fasting total cholesterol (mg/dl)	Postprandial total cholesterol (mg/dl)	Fasting LDL-C (mg/dl)	Postprandial LDL-C (mg/dl)
before therapy	219.1 ±37.0[a]	228.8 ±40.1[a]	124.0 ±41.9	107.8 ±39.7
after 6 weeks	185.7 ±45.8[c]	183.8 ±49.4[c]	99.5 ±38.9[b]	93.6 ±40.7
after 12 weeks	194.5 ±42.3[b]	199.8 ±46.0[b]	108.1 ±43.2	102.9 ±42.1
	fasting glucose (mg/dl)	postprandial glucose (mg/dl)	fasting hsCRP (mg/l)	postprandial hsCRP (mg/l)
before therapy	123.9 ±33.2[a]	124.1 ±37.9[a]	2.1 ±1.8	2.1 ±1.7
after 6 weeks	112.3 ±19.9	128.1 ±36.2	2.3 ±1.9	2.1 ±1.7
after 12 weeks	105.7±16.7[b]	117.5 ±37.2	1.6 ±1.0	1.5 ±1.0
	fasting TG (mg/dl)	postprandial TG (mg/dl)	fasting HDL-C (mg/dl)	postprandial HDL-C (mg/dl)
before therapy	254.4 ±137.2[a]	375.8 ±168.8[a]	41.0 ±11.3	40.0 ±1.9
after 6 weeks	206.5 ±124.1	235.3 ±123.7[c]	44.8 ±10.0	42.5 ±9.4
after 12 weeks	177.8 ±83.9[b]	222.6 ±126.8[c]	47.6 ±12.0[b]	46.9 ±13.1[b]
	fasting HDL_2-C (mg/dl)	postprandial HDL_2-C (mg/dl)	fasting HDL_3-C (mg/dl)	postprandial HDL_3-C (mg/dl)
before therapy	7.6 ±3.7	7.1 ±2.7[b]	33.4 ±10.5	32.2 ±9.7
after 6 weeks	9.1 ±4.6	7.3 ±4.6	35.6 ±7.6	35.4 ±7.8
after 12 weeks	9.7 ±5.3[b]	9.8 ±5.9[b]	37.8 ±8.7[b]	37.2 ±9.3[b]
	fasting apo A (g/dl)	postprandial apo A (g/dl)	fasting apo B (g/dl)	postprandial apo B (g/dl)
before therapy	1.4 ±0.3	1.4 ±0.2	1.1 ±0.3	1.1 ±0.3
after 6 weeks	1.4 ±0.3	1.4 ±0.3	1.0 ±0.2	0.9 ±0.2
after 12 weeks	1.5 ±0.2	1.5 ±0.2	1.0 ±0.2	4.5 ±1.9

Data are given as mean ± standard deviation.
a significant differences compared to the control group (with normolipemia); $p < 0.001$
b significant differences compared to baseline (before therapy) fasting or postprandial parameter levels; $p < 0.05$
c significant differences compared to baseline fasting (before therapy) or postprandial parameter levels; $p < 0.01$

Abbreviations: apo A – apolipoprotein A, apo B – apolipoprotein B, HDL-C – high-density lipoprotein cholesterol, hsCRP – high-sensitivity C-reactive protein, LDL-C – low-density lipoprotein cholesterol, TG – triglycerides

men (it was also observed in the control group after the meal). Moreover, in patients with DM there was a correlation between postprandial levels of TG and hsCRP after 12 weeks. Contrary to the control group, there were no associations between fasting or postprandial HDL_3-C and hsCRP levels in the DM and AH groups (TABLE 4). The analysis of relationships between particular variables showed that normalization of lipid profiles did not completely restore all the associations between fasting lipid and protein parameters observed in controls.

DISCUSSION In all diabetic men lipid levels were increased. Hypolipemic therapy reduced elevated lipid levels as expected. Statin administration led to a decrease in total cholesterol and LDL levels in men with DM and hypercholesterolemia. Such effect of statins has been convincingly demonstrated in randomized trials including UKPDS (United Kingdom Prospective Diabetes Study), CARE (Cholesterol and Recurrent Events), CARDS, 4S, HPS (Heart Protection Study), and LIPID.[9] Also fibrate has a beneficial effect on lipids, by reducing TG and increasing HDL-C levels, in both diabetic and nondiabetic patients, as confirmed in VA-HIT (Veterans Affairs HDL Intervention Trial) or FIELD (Fenofibrate Intervention and Event Lowering in Diabetes Study).[10] However, it is difficult to explain why LDL-C increased again after 12 weeks of statin therapy in men with subclinical hyperlipemia. The most valid explanation would be medication non-adherence, although not confirmed by any of the patients.

In the present study postprandial lipemia was calculated as changes in TG levels, induced by a standard high-fat meal, compared to fasting triglyceridemia ($\Delta TG = TG_p - TG_o$). Prior to hypolipemic therapy, the magnitude of changes in TG were more than twofold higher in DM patients compared to men with normolipemia or hyperlipemia and no DM. This finding indicates that abnormalities in TG homeostasis observed in diabetic patients, are likely caused by a number of factors, not only lipid disturbances. One

TABLE 3 Fasting and postprandial levels of lipids, glucose, C-reactive protein, apolipoprotein A and B in 27 men with hyperlipemia and no diabetes before and during hypolipemic therapy

	Fasting total cholesterol (mg/dl)	Postprandial total cholesterol (mg/dl)	Fasting LDL-C (mg/dl)	Postprandial LDL-C (mg/dl)
before therapy	221.2 ±38.9[a]	223.7 ±43.7[a]	123.0 ±37.8	114.5 ±41.9
after 6 weeks	199.1 ±37.3[b]	207.7 ±41.2	101.3 ±33.8[b]	103.3 ±36.9
after 12 weeks	215.6 ±52.5	215.6 ±45.1	118.0 ±29.3	111.5 ±29.8
	fasting glucose (mg/dl)	postprandial glucose (mg/dl)	fasting hsCRP (mg/l)	postprandial hsCRP (mg/l)
before therapy	97.0 ±23.3	98.4 ±24.8	2.1 ±1.8	2.0 ±1.9
after 6 weeks	95.6 ±16.2	97.4 ±14.3	1.7 ±1.7	1.7 ±1.6
after 12 weeks	97.3 ±20.1	105.5 ±21.0	1.4 ±0.9	1.4 ±0.9
	fasting TG (mg/dl)	postprandial TG (mg/dl)	fasting HDL-C (mg/dl)	postprandial HDL-C (mg/dl)
before therapy	269.5 ±148.9[a]	343.9 ±186.3[a]	44.8 ±11.2	43.1 ±10.7
after 6 weeks	250.5 ±187.6	317.0 ±199.3	47.4 ±13.7	45.8 ±13.0
after 12 weeks	222.2 ±165.8	259.2 ±175.6	50.2 ±16.6	48.6 ±14.7
	fasting HDL_2-C (mg/dl)	postprandial HDL_2-C (mg/dl)	fasting HDL_3-C (mg/dl)	postprandial HDL_3-C (mg/dl)
before therapy	9.1 ±6.5	7.2 ±5.0	35.7 ±7.5	36.1 ±8.0
after 6 weeks	10.4 ±5.5	8.9 ±4.8	36.5 ±11.1	36.6 ±11.0
after 12 weeks	10.7 ±8.2	13.9 ±19.4	39.3 ±11.0	38.7 ±13.0
	fasting apo A (g/dl)	postprandial apo A (g/dl)	fasting apo B (g/dl)	postprandial apo B (g/dl)
before therapy	1.5 ±0.3	1.5 ±0.2	1.2 ±0.3	1.2 ±0.2
after 6 weeks	1.5 ±0.2	1.4 ±0.2	1.0 ±0.2	1.0 ±0.2
after 12 weeks	1.5 ±0.3	1.4 ±0.3	1.1 ±0.3	1.1 ±0.2

Data are given as mean ± standard deviation.
a significant differences compared to the control group with normolipemia; $p < 0.001$
b significant differences compared to baseline (before therapy) fasting or postprandial parameter levels; $p < 0.05$

Abbreviations: see **TABLE 2**

of the apparent factors is insulin deficiency or resistance, which reduces the activity of lipases hydrolyzing TG-rich lipoproteins and enhances liver fatty acid uptake. The present study also demonstrated abnormal associations between TG and HDL in diabetic patients, i.e. between TG and HDL_3 subfraction, evident in the absence of inverse linear relationships between TG and HDL-C, or TG and HDL_3-C levels – correlations which were observed in normolipemic men and patients with hyperlipemia and no DM.

An inverse correlation between TG and HDL_3-C levels is beneficial in terms of the mechanisms which protect from accelerated atherosclerosis. HDL significantly inhibits platelet activation through acetylhydrolase and reduces thrombocyte aggregation as glycoprotein IIb/IIIa inhibitor. Moreover, HDL stimulates protein C and S activation. Only HDL_2 can act as a cofactor of the active protein C. On the other hand, oxidized forms of HDL_3 have procoagulant properties by activating plasminogen activator inhibitor type 1.[5,11] Thus, a decrease in HDL_3 levels accompanied by an increase in TG levels in nondiabetic men can be viewed as a mechanism that prevents atherosclerosis. This mechanism seems to be impaired in diabetic patients. Hypolipemic therapy significantly reduced postprandial lipemia and restored desirable correlations between TG and HDL-C or TG and HDL_3-C levels.

Similarly to Taskinen et al., we observed a positive correlation between TG and apo B levels.[3] The authors suggested that the production of TG and apo B contained in type-1 and -2 VLDL in diabetic patients was associated with apo B overproduction and a decreased ability of insulin to suppress the synthesis of type-1 VLDL. In the present study, the correlation between TG and apo B in diabetic men was observed after 6 weeks of treatment, and in some patients postprandial apo B levels increased after 12 weeks. The correlation between TG and apo B also occurred in AH men during treatment and in the control group (after the meal), and was not restricted only to diabetic subjects.

Hypolipemic therapy did not restore all relationships between variables in patients with DM. Correlations between TG and hsCRP levels (positive) or between HDL_3-C and hsCRP levels (inverse) did

TABLE Correlations between lipid (lipid and protein) levels measured at baseline, after 6 and 12 weeks of therapy in men with type 2 diabetes (DM), men with hyperlipemia and no diabetes (asymptomatic hyperlipemia – AH) and control subjects

Correlations between parameters	At baseline		After 6 weeks		After 12 weeks	
	0	P	0	P	0	P
DM (n = 26)						
TG – HDL-C	NS	NS	NS	NS	–0.54	NS
TG – HDL_3-C	NS	NS	NS	NS	–0.52	–0.38
TG – hsCRP	NS	NS	NS	NS	NS	0.40
HDL_3 – hsCRP	NS	NS	NS	NS	NS	NS
TG – apo B	NS	NS	0.46	NS	0.43	NS
apo B – LDL-C	0.36	0.46	0.48	NS	0.72	NS
apo A – HDL-C	0.61	0.49	0.42	0.57	NS	0.59
AH (n = 27)						
TG – HDL-C	–0.46	NS	–0.56	–0.51	–0.39	NS
TG – HDL_3-C	–0.38	NS	–0.60	–0.47	–0.36	–0.37
TG – hsCRP	NS	NS	NS	NS	NS	–0.42
HDL_3 – hsCRP	NS	NS	NS	NS	NS	NS
TG – apo B	NS	NS	NS	NS	0.53	0.47
apo B – LDL-C	0.46	0.26	NS	NS	0.57	0.66
apo A – HDL-C	0.66	0.69	NS	0.36	0.59	0.53
Controls (n = 60)						
TG – HDL-C	–0.32	NS	–	–	–	–
TG – HDL_3-C	–0.36	NS	–	–	–	–
TG – hsCRP	0.27	NS	–	–	–	–
HDL_3 – hsCRP	–0.29	–0.43	–	–	–	–
TG – apo B	NS	0.31	–	–	–	–
apo B – LDL-C	0.27	0.36	–	–	–	–
apo A – HDL-C	0.51	0.29	–	–	–	–

All numerical coefficients are statistically significant.

Abbreviations: P – postprandial, NS – nonsignificant, 0 – fasting, others – see TABLE 2

not occur, although hsCRP levels decreased from a mean value of 2.1 mg/l to 1.6 mg/l.

The occurrence of the above correlations in the control group is likely to be the consequence of an inverse correlation between TG and HDL_3-C levels. The correlations between TG or HDL-C and hsCRP are consistent with the hypothesis that TG has a pro-inflammatory activity while HDL has an anti-inflammatory activity.[11-13] Based on our study, it can be assumed that HDL_3 subfraction participates in an anti-inflammatory response. A postprandial inverse correlation between HDL_3 and hsCRP in normolipemic men is essential given the fact that hsCRP levels are unaltered following a meal. On the other hand, other investigators observed complement activation after a meal.[14,15]

Increased postprandial lipemia is believed to precede abnormal fasting lipemia.[16] The present study showed that high postprandial lipemia is associated with abnormal fasting lipemia in diabetic men, and is significantly reduced by hypolipemic therapy. In diabetic patients with fasting TG levels 150–400 mg/dl, statin administration was less effective than fibrate in reducing the postprandial increases in TG-rich lipoprotein levels.[17] The current study also demonstrated that the statin was less potent than the fibrate in men with DM. Of note, baseline TG levels in patients treated with statin or fibrate were below 400 mg/dl, thus the drug effect on postprandial lipemia was only slightly dependent on the fasting levels.

In conclusion, the results of our study confirmed that type 2 DM is associated with increased postprandial lipemia. One of the mechanisms behind this reaction could be disturbed interactions between lipid variables (TG and cholesterol present in HDL_3 subfraction) or between lipid and inflammatory parameters (TG and hsCRP). Hypolipemic therapy resulted in reduced postprandial lipemia in patients with diabetes and restored correlations between the parameters.

Detection of lipid intolerance using a postprandial lipemia test allows to identify diabetic individuals who require hypolipemic treatment. Acceptable levels of postprandial lipemia cannot be determined for the general population because they depend on fasting lipemia, the type of lipid disorders, and comorbidities.

REFERENCES

1 Carstensen M, Thomsen C, Gotzsche O, et al. Differential postprandial lipoprotein responses in type 2 diabetic men with and without clinical evidence of a former myocardial infarction. Rev Diabet Stud. 2004; 1: 175-184.

2 Tentolouris N, Stylianou A, Lourida E, et al. High postprandial triglyceridemia in patients with type 2 diabetes and microalbuminuria. J Lipid Res. 2007; 48: 218-225.

3 Taskinen MR. Diabetic dyslipidemia: from basic research to clinical practice. Diabetologia. 2003; 46: 733-749.

4 Cybulska B, Kłosiewicz-Latoszek L. [Management of atherogenic dyslipidemia in patients with metabolic syndrome or type 2 diabetes mellitus]. Poradnik Lekarza. 2005; 2: 56-64. Polish.

5 Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk. 1996; 3: 213-219.

6 Abdel-Maksoud MF, Hokanson JE. The complex role of triglycerides in cardiovascular disease. Semin Vasc Med. 2002; 2: 325-333.

7 Anderson RA, Evans ML, Ellis GR, et al. The relationships between post-prandial lipaemia, endothelial function and oxidative stress in healthy individuals and patients with type 2 diabetes. Atherosclerosis. 2001; 154: 475-483.

8 Rydén L, Standl E, Bartnik M, et al. Guidelines on diabetes, prediabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur Heart J. 2007; 28: 88-136.

9 Simes RJ, Hunt D, Kirby A, et al. Long-term effectiveness and safety of pravastatin in 9014 patients coronary heart disease and average cholesterol concentrations: the LIPID trial follow-up. Lancet. 2002; 350-387.

10 Hiukka A, Leinonen E, Jauhiainen M, et al. Long-term effects of fenofibrate on VLDL and HDL subspecies in participants with type 2 diabetes mellitus. Diabetologia. 2007; 50: 2067-2075.

11 Barter PJ, Puranik R, Rye KA. New insights into the role of HDL as an anti-inflammatory agent in the prevention of cardiovascular disease. Curr Cardiol Rep. 2007; 9: 493-498.

12 Undas A, Celińska-Löwenhoff M. Antiplatelet effects of micronized fenofibrate in subjects with dyslipidemia. Pol Arch Med Wewn. 2007; 117: 235-240.

13 Barter PJ, Rye KA, Clay MA, al. Antiatherogenic effect of high density lipoproteins mechanisms. Arteriosclerosis. 1997; 134: 285-290.

14 Alipour A, Plokker TWM, Sniderman AD, et al. The metabolic syndrome in relation to complement component 3 and postprandial lipemia in patients from an outpatient lipid clinic and healthy volunteers. Atherosclerosis. 2007; 190: 167-173.

15 Włodarczyk A, Strojek K. Glucose intolerance, insulin resistance and metabolic syndrome in patients with stable angina pectoris. Obesity predicts coronary atherosclerosis and dysglycemia. Pol Arch Med Wewn. 2008; 118: 719-726.

16 Jose G, Pedro C, Fernando GF, et al. Target organ damage and cardiovascular complications in patients with hypertension and type 2 diabetes in Spain: a cross sectional study. Diabetologia. 2006; 10: 1475-2840.

17 Iovine C, Lilli S, Gentile A, et al. Atorvastatin or fenofibrate on post-prandial lipemia in type 2 diabetic patients with hyperlipidemia. Eur J Clin Invest. 2006; 36: 560-565.

ARTYKUŁ ORYGINALNY

Lipemia poposiłkowa u mężczyzn z cukrzycą typu 2 w trakcie leczenia hipolipemizującego

Anna Skoczyńska, Bogusława Kreczyńska, Rafał Poręba

Katedra i Klinika Chorób Wewnętrznych, Zawodowych i Nadciśnienia Tętniczego, Akademia Medyczna, Wrocław

SŁOWA KLUCZOWE

cukrzyca typu 2, hiperlipemia, lipemia poposiłkowa

STRESZCZENIE

WPROWADZENIE Mechanizmy lipemii poposiłkowej w różnych stanach chorobowych wymagają wyjaśnienia.

CELE Celem badań była ocena funkcjonowania homeostatu lipidowego po obciążeniu standaryzowanym posiłkiem u mężczyzn z rozpoznaniem cukrzycy typu 2 (*diabetes mellitus* – DM). Analizowano także wpływ krótkotrwałego leczenia hipolipemizującego na lipemię poposiłkową.

PACJENCI I METODY Badaniem objęto 26 mężczyzn z DM w wieku 53 ±6,7 lat, 27 z hiperlipemią bez cukrzycy (bezobjawowa hiperlipemia – BH) i 60 z normolipemią w wieku 46 ±11 lat. U wszystkich badanych z DM występowała hiperlipemia na czczo, dlatego rozpoczęto leczenie simwastatyną (20 mg/dobę) lub fenofibratem (267 mg/dobę), podobnie jak w grupie mężczyzn z BH. Próbki krwi pobierano na czczo i 3 godziny po posiłku trzykrotnie, tj. na początku, po 6 i 12 tygodniach farmakoterapii. Oznaczano trójglicerydy (*triglycerides* – TG), glukozę, cholesterol całkowity, cholesterol LDL (*low-density lipoprotein cholesterol* – LDL-C) oraz HDL_2 (*high-density lipoprotein cholesterol* – HDL-C) i HDL_3 metodami rutynowymi, apolipoproteiny A i B immunoturbidymetrycznie, białko C-reaktywne (*high-sensitivity C-reactive protein* – hsCRP) metodą immunonefelometryczną.

WYNIKI U mężczyzn z DM zmiany stężenia triglicerydów indukowane przez posiłek (140 ±68,0 mg/dl) były większe niż u mężczyzn z normolipemią (62,1 ±52,5 mg/dl; $p < 0{,}001$) lub w grupie BH (76.3 ±80 mg/dl; $p < 0{,}05$). Nie stwierdzono liniowej zależności między stężeniami TG (lub HDL-cholesterolu) a HDL_3 cholesterolu, ani między stężeniami TG a hsCRP u chorych na DM. Leczenie hipolipemizujące obniżyło stężenia lipidów i hsCRP na czczo. Ponadto spowodowało istotną ($p < 0.001$) redukcję lipemii poposiłkowej i przywrócenie niektórych zależności między parametrami lipidowymi obserwowanymi w grupie kontrolnej, ale nie korelacji z hsCRP.

WNIOSKI Cukrzyca typu 2 jest związana ze zwiększoną lipemią poposiłkową i zaburzeniami w homeostazie lipidów. Wykrycie nietolerancji tłuszczów w teście lipemii poposiłkowej może być wskazaniem do leczenia hipolipemizującego.

Adres do korespondencji:
prof. dr hab. Anna Skoczyńska, Katedra i Klinika Chorób Wewnętrznych, Zawodowych i Nadciśnienia Tętniczego, Akademia Medyczna, ul. Pasteura 4, 50-367 Wrocław, tel.: 0-71-784-25-22, fax: 0-71-327-09-54, e-mail: annaskoc@ak.am.wroc.pl

Praca wpłynęła: 09.04.2009.
Przyjęta do druku: 02.06.2009.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2009; 119 (7-8): 461-468