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Postprandial Lipemia and C-Reactive Protein in Middle-Aged Men Treated for Hyperlipemia

Lipemia poposiłkowa i białko C-reaktywne u mężczyzn w średnim wieku leczonych z powodu hiperlipemii

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Abstract

Background. Postprandial lipoproteins enhance inflammatory activity, but the mechanisms of this action remain unclear.
Objectives. The aim of the study was to determine postprandial lipemia in hyperlipemic subjects and to study the relationship between lipids and high-sensitivity C-reactive protein (hs-CRP) in fasted and postprandial states.
Material and Methods. Blood samples were taken from 148 men (60 normolipemic, 27 hypertriglyceridemic, 49 hypercholesterolemic, and 12 with mixed hyperlipemia) in a fasted state and three hours after a standardized high-fat meal (1500 kcal) three times: before and after 6 and and 12-weeks of therapy with simvastatin (20 mg/ /day) and/or fenofibrate (267 mg/day). Triglycerides (TG), total lipoprotein, low-density lipoprotein (LDL), high--density lipoprotein (HDL), and HDL_2- and HDL_3-cholesterol were measured by routine methods, apolipoproteins A and B by immunoturbidimetry, and hs-CRP by immunonephelometry.
Results. At the start of the study the mean hs-CRP level was increased ($p < 0.05$) in the hyperlipemic vs. the normolipemic men whereas the mean postprandial triglyceride increase (ΔTG) was higher ($p < 0.05$) in the men with hypertriglyceridemia. However, fasting TG (TG_o) > 400 mg/dl was associated with low ΔTG and TG_o < 400 mg/dl with high TG changes. Hypolipemic therapy caused a reduction in postprandial TG changes in all the hyperlipemic men. Linear correlation between the concentrations of TG and HDL as well as HDL_3-cholesterol was found. Positive correlation between TG_o and hs-CRP concentrations coexisted with a negative relationship between HDL_3-cholesterol and hs-CRP only in the control group. Statin restored the relationship between the concentrations of HDL_3-C and hs-CRP in the hypercholesterolemic men.
Conclusions. Increased postprandial lipemia in hyperlipemic men was associated with increased inflammatory activity and HDL_3-cholesterol seems to have anti-inflammatory properties. Hypolipemic therapy decreased postprandial lipemia and at least partially recovered regulatory function in lipid homeostasis (**Adv Clin Exp Med 2010, 19, 1, 89–98**).

Key words: postprandial lipemia, C-reactive protein, statin, fibrate, hyperlipemia.

Streszczenie

Wprowadzenie. Lipemia poposiłkowa jest związana ze wzrostem aktywności zapalnej, chociaż mechanizm tego związku jest niejasny.
Cel pracy. Określenie lipemii poposiłkowej u osób z hiperlipemią i ocena zależności występujących między lipidami i wysoko czułym białkiem C-reaktywnym (hsCRP) w warunkach przed i po posiłku.
Materiał i metody. Badaniem objęto 148 mężczyzn (60 normolipemicznych, 27 z hipertrójglicerydemią, 49 z hipercholesterolemią i 12 z mieszaną hiperlipemią). Próbki krwi pobierano na czczo oraz po 3 godzinach od spożycia standaryzowanego posiłku wysokotłuszczowego (1500 kcal) 3-krotnie: przed, po 6 i po 12 tygodniach terapii simwastatyną (20 mg/dobę) i/lub fenofibratem (267 mg/dobę). Trójglicerydy (TG), cholesterol (całkowity, LDL, HDL, HDL_2 i HDL_3) oznaczano metodami rutynowymi, apolipoproteiny A and B immunoturbidymetrycznie, a hsCRP immunonefelometrycznie.
Wyniki. Na początku badania średnie stężenie hsCRP u mężczyzn z hiperlipemią było większe ($p < 0,05$) niż u mężczyzn z normolipemią, poposiłkowe zwiększenie stężenia trójglicerydów (ΔTG) natomiast był większe ($p < 0,05$) u mężczyzn z hipertriglyceridemią. Jednocześnie wartościom TG na czczo (TG_o) > 400 mg/dL towa-

rzyszyły mniejsze ΔTG, podczas gdy TG_o < 400 mg/dL były związane z większymi poposiłkowymi zmianami TG. Leczenie hipolipemizujące istotnie ograniczało lipemię poposiłkową. Wykazano występowanie liniowych zależności między stężeniami TG a HDL lub HDL_3-cholesterolu. Dodatnia korelacja między TG_o i hsCRP współistniała z ujemną zależnością między HDL_3-cholesterolem a hsCRP tylko w grupie kontrolnej. Statyna przywracała zależność między stężeniami HDL_3-C a hsCRP u mężczyzn z hipercholesterolemią.
Wnioski. Zwiększona lipemia poposiłkowa u mężczyzn leczonych z powodu hiperlipemii jest związana ze zwiększoną aktywnością zapalną, a subfrakcja HDL_3 wydaje się mieć właściwości przeciwzapalne. Leczenie hipolipemizujące zmniejsza lipemię poposiłkową i przynajmniej częściowo przywraca prawidłowe funkcje regulacyjne w homeostazie lipidów (**Adv Clin Exp Med 2010, 19, 1, 89–98**).

Słowa kluczowe: lipemia poposiłkowa, białko C-reaktywne, statyna, fibrat, hiperlipemia.

The atherogenic activity of postprandial lipoproteins is documented. Triglyceride (TG)-rich chylomicrones and their remnants deliver substrates to generate very-low-density lipoproteins (VLDLs) in the liver. The increased large VLDL1 particles initiate a sequence of events that generates atherogenic remnants, small dense LDL and small dense HDL particles [1]. Remnant-like particles (RLPs) penetrate the intact endothelium, undergo modification in the subendothelial space, and are taken up via scavenger receptors located on the surface of macrophages. In this way, RLPs can directly participate in foam-cell formation [2–4]. Consisting of high amounts of medullar TG, RLPs undergo lypolysis by lipoprotein lipase on the surface of macrophages [5]. Lysolecithin, formed from the product of lipolysis, together with free fatty acids can stimulate chemotaxis of macrophages, up-regulate the expression of adhesion molecules on the endothelium, and activate the expression of growth factors [6]. In this manner, lipolysis can indirectly stimulate foam-cell formation and inflammation [5, 7]. Postprandial lipoproteins can also stimulate an inflammatory reaction in vessel walls, activating leukocytes and the complement system [8] as well as disturbing nitric oxide metabolism [9].

Increased fasting TG level is a known factor independently associated with increased cardiovascular risk. Increased postprandial lipemia contributes to the excess risk of future coronary events [1, 10] and is associated with frequent occurrence of asymptomatic carotid atherosclerosis [11] and has been shown to be an independent prognostic marker of coronary heart disease as well as the severity of the disease [12]. Hypertriglyceridemia together with decreased HDL, composing atherogenic dyslipidemia, is responsible for residual cardiovascular risk [13–16].

Hypolipemic therapy decreases postprandial lipemia and attenuates inflammatory activity in hyperlipemic patients [17, 18]. Rosuvastatin also reduces serum lipids and high-sensitivity C-reactive protein (hs-CRP) and significantly reduces cardiovascular incidence in normolipemic subjects, which is why the JUPITER study was interrupted [19]. Fibrates, acting as PPAR alpha agonists, reduce postprandial TG and fasting inflammatory potential in patients with atherogenic dyslipidemia [20, 21]. However, the relationship between lipids and hs-CRP, especially in the postprandial state, is unclear.

In this study, disturbances in postprandial lipid homeostasis and changes in inflammatory activity in men diagnosed with hyperlipemia were evaluated. The aim of the study was to determine the relationship between fasting/postprandial lipids and hs-CRP in men diagnosed with hypercholesterolemia or hypertriglycerydemia before and during treatment with a statin and/or a fibrate.

Material and Methods

Patients

Men in the age 50.9 ± 9.6 years with diagnosed hyperlipemia who had not been treated with hypolipemic drugs for at least the past three months and normolipemic volunteers (45.6 ± 11.2 years old) were involved in the study. Exclusion criteria included liver, renal, thyroid, inflammatory, and neoplastic diseases. Of the 88 patients with hyperlipemia, 49 (52.1 ± 9.6 years old) were diagnosed with hypercholesterolemia (defined by the National Cholesterol Education Program as a fasting total cholesterol level of > 200 mg/dl, 27 (48.7 ± ± 10.9 years old) with hypertriglyceridemia (defined by the NCEP as a fasting TG level of > 200 mg/dl), and 12 (51.4 ± 4.8 years old) with mixed hyperlipidemia. According to the European Society of Cardiology/Polish Society of Cardiology guideline (2007), the patients were treated with a simvastatin (Simvasterol, Polpharma) at a dose of 20 mg and/or fenofibrate (Lipanthyl, Solvay) at a dose of 267 mg daily.

Apart from physical examination, biochemical measurements in blood were carried out in fasted and postprandial states: 1) at the beginning, 2) after 6 weeks, and 3) after 12 weeks of the phar-

macotherapy. The parameters were determined in fasted and fed states also in 60 normolipemic men (control group). Each time, samples of blood were taken 12 hours after the last meal and 3 hours after the standardized lipid-rich meal (100 g of fat, 1500 kcal). The fat composition of this meal was determined by gas chromatographic and mass spectroscopic methods and they showed: C 18 : 1 41.4% oleic acid, C 16:0 24.7% palmitic acid, C 18 : 0 16.7% stearic acid, C 18:2 8.8% linolic acid, and 9.3% other.

Written informed consent was obtained from all the men taking part in the study. The study was approved by Local Ethics Committee in Wroclaw and followed the Declaration of Helsinki.

Biochemical Measurements

Serum total cholesterol, TG, and HDL--cholesterol (HDL-C) were measured using the Spinreact enzymatic assay (Sant Esteve De Bas, Girona, Spain). LDL cholesterol (LDL-C) was calculated by the Friedewald formula. The Quantolip HDL test (Technoclone GmbH, Vienna, Austria) was used to precipitate HDL_2- and HDL_3--cholesterol. Apolipoprotein A (apo A) and apolipoprotein B (apo B) were determined in serum with the immunoturbidimetric method of DADE Behring Marburg GmbH (Marburg, Germany). Serum hs-CRP was determined using the CardioPhase hs-CRP Dade Behring preparation with the molecular immunonephelometric method according to the N Rheumatology Standard SL (BCR-CRM 470).

Statistical Analysis

Statistical analysis was performed with the use of the Statistica PL 6.0 program (Stat Soft, Poland). Means (x) and standard deviations (SD) are given except for Fig. 1, in which means and standard error of means (SEM) are presented. The distribution of the variables was checked with the Shapiro-Wilk W test. The ANOVA Friedman test was then used because the variables had nonparametric distributions. Statistically significant differences between means were determined with the Scheffe or NIR post-hoc test. Values of $p < 0.05$ were accepted as statistically significant. Correlations between parameters were checked by Spearman's correlation coefficient.

Results

The basal characteristics of all the groups are presented in Table 1. There were no differences among the patient groups regarding body mass index and smoking habit. During hypolipemic therapy, no adverse clinical and/or biochemical symptoms were observed.

After 6 weeks of treatment with the statin, mean fasting LDL-C levels decreased ($p < 0.001$) and this effect was maintained up to the end of

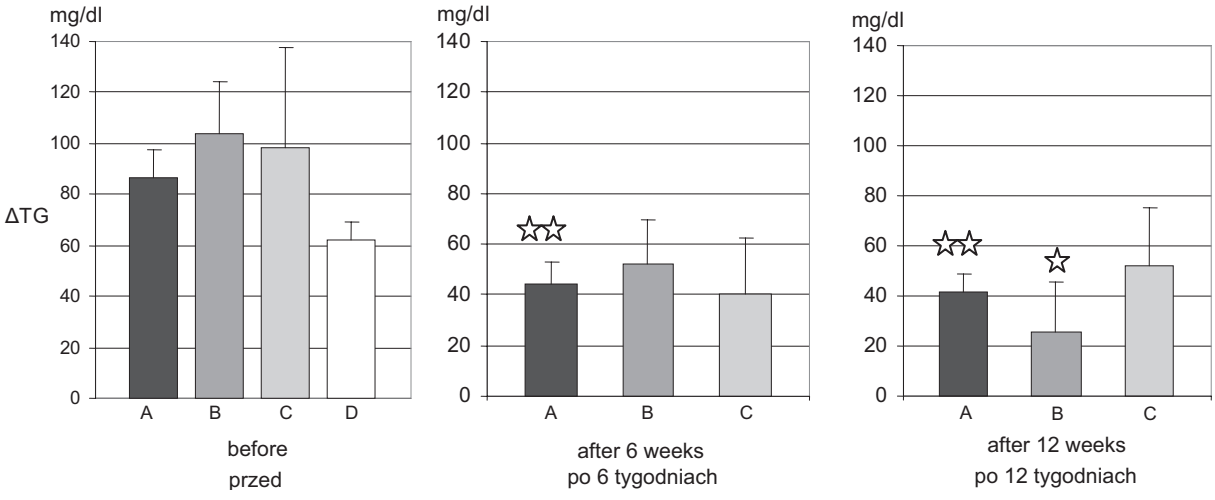

Fig. 1. Mean absolute postprandial increase in TG (ΔTG = postprandial TG minus fasting TG). Results are given as means and *SEM*, A) in men treated with a statin (n = 49), B) with a fibrate (n = 27), C) with a statin plus fibrate (n = = 12), and D: in the control group (n = 60). In men treated with a statin, ** $p < 0.01$, differences statistically significant compared with the period before the treatment; in men treated with a fibrate, * $p < 0.05$, difference statistically significant compared with the period before the treatment

Ryc. 1. Średnie bezwzględne poposiłkowe wzrosty TG (ΔTG = poposiłkowe TG minus TG na czczo). Wyniki przedstawiono jako średnia ± SEM. U mężczyzn leczonych statyną (A; n = 49), fibratem (B; n = 27), statyną i fibratem (C; n = 12) i w grupie kontrolnej (D; n = 60). [a]: w grupie mężczyzn leczonych statyną: ** p < 0,01 – różnica statystycznie istotna w porównaniu do okresu sprzed leczenia; w grupie mężczyzn leczonych fibratem: * p < 0,05 – różnica statystycznie istotna w porównaniu do okresu sprzed leczenia

Table 1. Baseline characteristics of 88 men in groups intended to be treated with a statin, a fibrate, or a statin plus a fibrate and 60 normolipemic men (control group). Results are given as means ± *SD*. There are significant differences compared with the control group: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Tabela 1. Wyjściowa charakterystyka grupy 88 mężczyzn mających rozpocząć leczenie statyną, fibratem, statyną plus fibratem i grupy mężczyzn normolipemicznych (kontrolnej). Wyniki przedstawiono jako średnią ± SD. Zaznaczono różnice statystycznie istotne w odniesieniu do grupy kontrolnej: * $p < 0{,}05$, ** $p < 0{,}01$, *** $p < 0{,}001$

Variable (Zmienna)	Statin (Statyna) n = 49	Fibrate (Fibrat) n = 27	Statin + fibrate (Statyna + fibrat) n = 12	None (Bez leków) n = 60
Before the treatment (Przed leczeniem)				
BMI (kg/m^2)	29.3 ± 5.4	31.0 ± 5.2	28.9 ± 5.4	28.9 ± 5.2
Smoker (%) (Palacze)	21 (43 %)	15 (56 %)	6 (50%)	18 (30%)
Triglyceride (mg/dl) (Trójglicerydy)	171.6 ± 55.4	315.1 ± 113.3**	452.4 ± 196.9***	131.9 ± 49.4
LDL-cholesterol (mg/dl)	140.6 ± 37.9	101.7 ± 33.4	130.5 ± 28.9	110.0 ± 36.7
HDL-cholesterol (mg/dl)	46.8 ± 13.6	40.2 ± 9.8	45.5 ± 11.3	44.4 ± 8.5
Apolipoprotein A (g/l) (Apolipoproteina)	1.5 ± 0.3	1.4 ± 0.3	1.8 ± 0.4	1.5 ± 0.3
Apolipoprotein B (g/l) (Apolipoproteina)	1.2 ± 0.3	1.1 ± 0.2	1.4 ± 0.3	1.1 ± 0.3
hs-CRP (mg/l)	2.6 ± 2.4*	2.3 ± 1.9*	2.8 ± 1.7*	1.6 ± 1.9

the 12th week. Therapy with the fibrate resulted in a gradual reduction in mean fasting TG level, so that after 12 weeks it was significantly lower ($p < 0.001$). Statin plus fibrate administration decreased fasting LDL-C after 6 weeks ($p < 0.05$) and TG concentrations after 12 weeks ($p < 0.05$). The effect of the pharmacotherapy on HDL-C, apo A, apo B, and hs-CRP was similar in all the groups of men with hyperlipemia (Table 2).

At the start of the study the mean absolute postprandial increase in TG (postprandial TG minus fasting TG: $\Delta TG = TG_p\text{-}TG_o$) in the men with hypertriglyceridemia (103.7 ± 107.0 mg/dl) was higher ($p < 0.05$) than in the normolipemic men (67.5 ± 57.5 mg/dl). Mean ΔTG in the men diagnosed with mixed hyperlipemia (98.1 ± 136.7 mg/dl) or hypercholesterolemia (86.7 ± 78.9 mg/dl) was slightly higher than in the control group. Hypolipemic therapy had a significant effect on postprandial lipemia. In the men with hypercholesterolemia, the statin significantly ($p < 0.01$) reduced high-fat meal-stimulated increases in TG after 6 weeks, but in the patients with hypertriglyceridemia, the fibrate reduced ($p < 0.05$) postprandial ΔTG after 12 weeks (Fig. 1). However, the relative effects of the drugs on postprandial lipemia (expressed as the percentage of fasting lipemia) were similar; after 6 weeks of treatment with the statin, the postprandial triglyceridemia reduction (from 51% of to 36% TG_o) was similar to that induced by the fibrate (from 39% to 24% TG_o) and this effect was maintained until the 12th week of therapy (Table 3). This observation needs to be completed by analysis of the dependency between fasting and inducible (postprandial) values of TG. Linear regression analysis confirmed a strong positive correlation between TG_o and TG_p before treatment (Fig. 2), after 6 weeks of therapy ($r = 0.882$, $p < 0.001$), and at the end of the study ($r = 0.913$, $p < 0.001$). However, variable distribution analysis show that high TG_o values (> 400 mg/dl) were associated with low meal-induced changes in TG (ΔTG), whereas normal or slightly elevated TG_o values (<400 mg/dl) were associated with higher TG changes in the fed state (Fig. 3).

Regression analysis performed for the data obtained from all the groups of men showed linear relationships between apo B and LDL-C ($r = 0.345$, $p < 0.001$ and $r = 0.383$, $p < 0.001$, respectively, for fasting and postprandial values), apo A and HDL-C ($r = 0.499$, $p < 0.001$ and $r = 0.452$, $p < 0.001$), and also between fasting TG and HDL-C concentrations ($r = -0.256$, $p < 0.001$).

As shown in Table 4, such linear dependencies were found in the group of normolipemic

Table 2. The effect of 6-week and 12-week therapy with statin, fibrate, or both on fasting lipid, apolipoprotein, and hs-CRP concentrations in the serum of men with hyperlipemia. Results are presented as means ± *SD*. There are significant differences compared with the basal values (measured before the treatment): * $p < 0.05$, *** $p < 0.001$

Tabela 2. Wpływ 6- i 12-tygodniowej terapii statyną, fibratem lub terapii złożonej na wskaźniki oznaczane na czczo: stężenie lipidów, apolipoprotein i hsCRP w surowicy mężczyzn z hiperlipemią. Wyniki przedstawiono jako średnia ± SD. Zaznaczono różnice statystycznie istotne w odniesieniu do wartości wyjściowych (oznaczonych przed rozpoczęciem leczenia): * $p < 0{,}05$, *** $p < 0{,}001$

Variable (Zmienna)	Statin (Statyna) n = 49	Fibrate (Fibrat) n = 27	Statin + fibrate (Statyna + fibrat) n = 12
Before treatment (Przed leczeniem)			
TG (mg/dl)	171.6 ± 55.4	315.1 ± 113.3	452.4 ± 196.9
T-CHOL (mg/dl)	225.8 ± 32.8	200.1 ± 29.3	267.2 ± 38.5
LDL-C (mg/dl)	140.6 ± 37.9	101.7 ± 33.4	130.5 ± 28.9
HDL-C (mg/dl)	46.8 ± 13.6	40.2 ± 9.8	45.5 ± 11.3
HDL_2-C (mg/dl)	9.1 ± 5.9	8.8 ± 6.2	9.6 ± 3.3
HDL_3-C (mg/dl)	37.7 ± 10.1	32.8 ± 7.9	35.9 ± 10.2
Apo-A (g/l)	1.5 ± 0.3	1.4 ± 0.3	1.8 ± 0.4
Apo-B (g/l)	1.2 ± 0.3	1.1 ± 0.2	1.4 ± 0.3
CRP (mg/l)	2.6 ± 2.4	2.3 ± 1.9	2.8 ± 1.7
After 6 weeks of treatment (Po 6 tygodniach leczenia)			
TG (mg/dl)	158.0 ± 69.4	268.6 ± 159.6	312.9 ± 218.0
T-CHOL (mg/dl)	189.5 ± 44.1	195.5 ± 29.2	204.6 ± 50.8
LDL-C (mg/dl)	109.6 ± 38.8***	98.0 ± 30.8	89.2 ± 30.6*
HDL-C (mg/dl)	49.0 ± 14.7	42.8 ± 9.9	46.7 ± 9.2
HDL_2-C (mg/dl)	9.98 ± 6.2	8.74 ± 4.5	10.07 ± 3.6
HDL_3-C (mg/dl)	38.9 ± 10.9	33.7 ± 10.1	36.4 ± 8.1
Apo-A (g/l)	1.53 ± 0.34	1.41 ± 0.24	1.70 ± 0.29
Apo-B (g/l)	1.09 ± 0.26	1.06 ± 0.22	1.22 ± 0.26
CRP (mg/l)	2.26 ± 2.36	2.37 ± 1.94	2.14 ± 1.12
After 12 weeks of treatment (Po 12 tygodniach leczenia)			
TG (mg/dl)	156.6 ± 91.3	206.1 ± 122.4***	296.2 ± 180.4*
T-CHOL (mg/dl)	192.7 ± 34.1	204.6 ± 56.7	240.0 ± 48.4
LDL-C (mg/dl)	110.2 ± 30.2***	110.8 ± 39.7	124.6 ± 44.3
HDL-C (mg/dl)	51.7 ± 17.0	44.9 ± 11.6	48.2 ± 10.6
HDL_2-C (mg/dl)	11.9 ± 8.7	9.1 ± 5.4	10.3 ± 3.2
HDL_3-C (mg/dl)	39.8 ± 11.1	35.8 ± 8.4	39.2 ± 9.5
Apo-A (g/l)	1.50 ± 0.34	1.45 ± 0.27	1.60 ± 0.27
Apo-B (g/l)	1.07 ± 0.29	1.06 ± 0.19	1.27 ± 0.45
CRP (mg/l)	1.89 ± 2.08	1.67 ± 1.38	2.34 ± 1.56

men, but not in the separate groups of men with hypercholesterolemia or hypertriglyceridemia (because of the small mixed-hyperlipemic group, the analysis is not presented). However, in each group, in the fasted and fed states, precise conjunction between two linear correlation, i.e. between TG and HDL-cholesterol and between TG and HDL_3-cholesterol, was observed (the presence or lack of correlation between the levels of TG and HDL-C was connected with the presence or lack a relationship between the concentrations of TG and HDL_3-C). On the other hand, only in the control group was there coexistence: positive linear correlation between fasting TG and hs-CRP levels and negative linear correlation between fasting HDL_3-C and hs-CRP level was shown (Table 4). This coexistence may arise from the reverse relationship between fasting TG and HDL_3-C concentrations in this group. However, no correlation between fasting TG or HDL_3-C and hs-CRP was observed in any group of men with hyperlipemia at the start of the study although the mean fasting hs-CRP concentration was greater than in healthy men (Table 1). The hypolipemic treatment reduced hs-CRP in all the studied groups (Table 2).

Table 3. Percent changes (from fasting) of postprandial concentrations of the parameters (95% confidence intervals) in men with hyperlipemia before, after 6 weeks, and after 12 weeks of the therapy with a statin and/or fibrate and in the controls

Tabela 3. Procentowe zmiany (w odniesieniu do oznaczanych na czczo) poposiłkowych stężeń wskaźników (95% przedział ufności): przed, po 6 i po 12 tygodniach leczenia statyną, fibratem lub obydwoma lekami mężczyzn z hiperlipemią oraz w grupie kontrolnej

Variable (Zmienna)	Statin (Statyna) n = 49	Fibrate (Fibrat) n = 27	Statin + fibrate (Statyna + fibrat) n = 12	None (Bez leków) n = 60
Before treatment (Przed leczeniem)				
TG	+51.2 (+39, +62)	+39.1 (19.7, +58.5)	+32.4 (+6.8, +57.9)	+58.3 (+45.1, +71.5)
T-Chol	+1.9 (−.10, +3.8)	+6.1 (−0.47, +12.8)	+3.4 (−2.5, +9.2)	+7.5 (+3.2, +11.7)
LDL-C	−9.9 (−14, −5.6)	−16.5 (−25.7, −7.4)	−8.5 (−18.8, +1.8)	−5.1 (−9.7, −0.54)
HDL-C	−3.0 (−6.0, −.03)	−1.4 (−5.7, +2.8)	+4.9 (−6.0, +15.9)	−1.7 (−5.0, +1.5)
HDL_2-C	+13.8 (−7.5, +35)	+24.5 (20.7, +69.8)	−12.9 (−42.5, +6.6)	+76.2 (10.2, +142.3)
HDL_3-C	−3.3 (−6.9, +0.4)	−3.2 (−7.7, +1.1)	+6.9 (−3.9, +17.8)	+1.8 (−5.5, +9.2)
Apo-A	+0.67 (−2.2, +3.5)	+0.61 (−2.9, +4.1)	−1.9 (−6.9, +2.9)	+2.1 (−2.2, +6.5)
Apo-B	+0.31 (−1.0, +11.6)	+1.7 (−4.8, +8.4)	−5.2 (−9.8, −0.70)	−2.8 (−7.9, +2.2)
CRP	−1.8 (−5.1, +1.4)	−5.2 (−13.1, +2.7)	+7.8 (−11.4, +27.1)	+1.3 (−6.4, +9.1)
After 6 weeks of treatment (Po 6 tygodniach leczenia)				
TG	+35.8 (+22.0, +49.6)	+24.1 (+11.7, 36.5)	+21.3 (+3.7, +38.9)	
T-Chol	+2.6 (−1.6, +6.8)	+3.1 (−0.07, +6.3)	+7.7 (−4.6, +19.9)	
LDL-C	−3.2 (−10.9, +4.5)	−1.2 (−17.0, +14.6)	+11.4 (−21.1, 44.0)	
HDL-C	−3.5 (−7.1, −.02)	−0.98 (−7.3, +5.4)	−1.1 (−4.4, +2.2)	
HDL_2-C	+16.9 (−26.9, +60.8)	+10.8 (−27.3, 48.9)	−12.3 (−40.9, 16.2)	
HDL_3-C	−0.6 (−4.0, +2.8)	+4.2 (−4.2, +12.5)	+1.9 (−4.5, +8.5)	
Apo-A	−1.5 (−4.9, +1.9)	−1.4 (−6.4, +3.4)	−0.8 (−9.8, +8.2)	
Apo-B	−3.3 (−6.8, +0.17)	+0. 35 (−5.1, +5.8)	−2.8 (−10.8, +5.1)	
Glucose	+7.3 (+2.3, +12.3)	+6.5 (−2.5, +15.5)	+12.4 (−3.3, +28.1)	
CRP	+7.9 (−3.7, +19.7)	−7.7 (−14.6, −1.3)	−2.8 (−8.4, +2.9)	
After 12 weeks of treatment (Po 12 tygodniach leczenia)				
TG	+33.6 (+21.6, +45.5)	+21.3 (+3.5, +39.1)	+19.1 (+0.72, 37.6)	
T-Chol	+1.2 (−0.54, +2.9)	+3.4 (−0.35, +7.1)	−0.4 (−4.8, +3.9)	
LDL-C	−4.4 (−7.8, −1.1)	−2.6 (−10.1, +4.9)	+1.1 (−24.7, +27.0)	
HDL-C	−3.1 (−6.1, −0.29)	+1.8 (−4.2, +7.8)	+1.7 (−7.7, +11.3)	
HDL_2-C	−2.5 (−14.3, +9.2)	+11.4 (−77.0, 30.6)	−12.2 (−55.0, 30.5)	
HDL_3-C	+0.40 (−2.5, +3.3)	−0.21 (−7.6, +7.1)	+3.5 (−3.8, +10.8)	
Apo-A	−2.7 (−7.6, +2.2)	−0.56 (−4.7, +3.6)	+5.4 (−7.4, +18.3)	
Apo-B	−1.7 (−6.6, +3.1)	+0.48 (−2.3, +3.3)	+7.7 (−7.0, +22.5)	
CRP	−2.3 (−7.5, +2.8)	+1.9 (−2.1, +5.9)	+3.8 (−7.5, +15.2)	

Discussion

The greater postprandial TG changes in hypertriglyceridemic vs. normolipemic men observed in this study were also observed in other studies of patients with atherogenic dyslipidemia [22–24]. However, in the present study the relative TG changes (expressed as the percentage of fasting TG) in the men with hypertriglyceridemia (39% of TG_o) were lower than in the control group (58% TG_o). In the men diagnosed with hypercholesterolemia, the direct increase in TG induced by the meal (86.7 ± 78.9 mg/dl) and the relative TG changes (51% TG_o) were similar to those of the control group (67.5 ± 57.5 mg/dl and 58% TG_o). The present authors supposed that postprandial TG changes, regardless of the type of hyperlipemia, depended on the fasting TG value. This can be explained on the basis of lipid homeostasis functioning as a system of limited capacity. Such a system allows some changes dependent on the initial values, and together with higher basal value admits smaller rises. The impaired synthesis and/or transport or activation of lipases (lipoprotein, hepatic, and/or endothelial lipase) can be these factors which limit the capacity TG homeo-

Table 4. Correlations between parameters measured before, after 6 weeks, and after 12 weeks of therapy in the men with hyperlipemia and in the control group (0 – in the fasted state, P – in the fed state). All correlation coefficients were statistically significant ($p < 0.05$); ns – not significant

Tabela 4. Zależności między wskaźnikami oznaczanymi przed, po 6 i po 12 tygodniach leczenia mężczyzn z hiperlipemią oraz w grupie kontrolnej (O – na czczo, P – po posiłku)

Correlation between (Zależności między)	Before treatment (Przed leczeniem)		After 6 weeks (Po 6 tygodniach)		After 12 weeks (Po 12 tygodniach)	
	0	P	0	P	0	P
Hypercholesterolemia (n = 49) (Hipercholesterolemia)						
TG – HDL-C	ns	ns	–0.31	ns	–0.40	–0.34
TG – HDL_3-C	ns	ns	–0.29	ns	–0.37	–0.31
TG – hsCRP	ns	ns	ns	ns	ns	ns
HDL_3 – hsCRP	ns	–0.30	ns	–0.33	–0.34	–0.33
TG – Apo B	ns	ns	ns	ns	ns	ns
Apo B – LDL	0.37	0.37	0.53	0.47	0.58	ns
Apo A – HDL	0.36	0.33	0.53	0.64	0.58	0.64
Hypertriglyceridemia (n = 27) (Hipertrójglicerydemia)						
TG – HDL-C	–0.40	ns	–0.55	ns	–0.43	–0.48
TG – HDL_3-C	–0.39	ns	–0.58	ns	–0.41	–0.54
TG – hsCRP	ns	ns	ns	ns	ns	ns
HDL_3 – hsCRP	ns	ns	ns	ns	ns	ns
TG – Apo B	ns	ns	ns	ns	ns	ns
Apo B – LDL	ns	ns	ns	0.63	0.65	0.71
Apo A – HDL	0.77	0.81	0.51	ns	0.43	0.46
Control (n = 60) (Grupa kontrolna)						
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	0.27	0.36	–	–	–	–
Apo A – HDL	0.51	0.29	–	–	–	–

static system. Small values of meal-induced ΔTG in patients with initial levels of TG > 400 mg/dl (Fig. 3) may support this hypothesis.

The statin or fibrate or both, beyond their typical effects on the fasting lipid pattern, reduced postprandial lipemia in all the studied hyperlipemic men. In other studies, statins lowered postprandial lipemia [25–28] and they appeared to be less effective than fibrate [29]. In the present study the effect of the statin was comparable to that induced by the fibrate. However, the effect of the statin was assessed in a population with lower values of TG_o than in the case of the fibrate. It is supposed that in men with a high fasting TG value, the effect of hypolipemic therapy on postprandial lipemia can be lower.

Postprandial triglyceridemia is closely related to fasting triglyceridemia and inversely related to HDL-cholesterol [30–33]. Also in the the present study a strong positive linear correlation between fasting and postprandial TG levels ($p < 0.001$) as well as a negative correlation between fasting TG and HDL-cholesterol ($p < 0.001$) were shown. The study also demonstrated that fasting or postprandial TG metabolism is related rather to HDL_3- than HDL_2-cholesterol. The protective role of HDL in the arterial wall is undisputed. However, the HDL_3 subfraction dominant in plasma displays properties associated with its chemical composition. Apo A-I-poor HDL_3 can accelerate atherosclerosis [34, 35]. An increased fasting HDL_3 level was observed during cuprofibrate or fenofibrate treatment [36, 37] and after 12 weeks of treatment with fenofibrate and/or simvastatin in this study (Table 2).

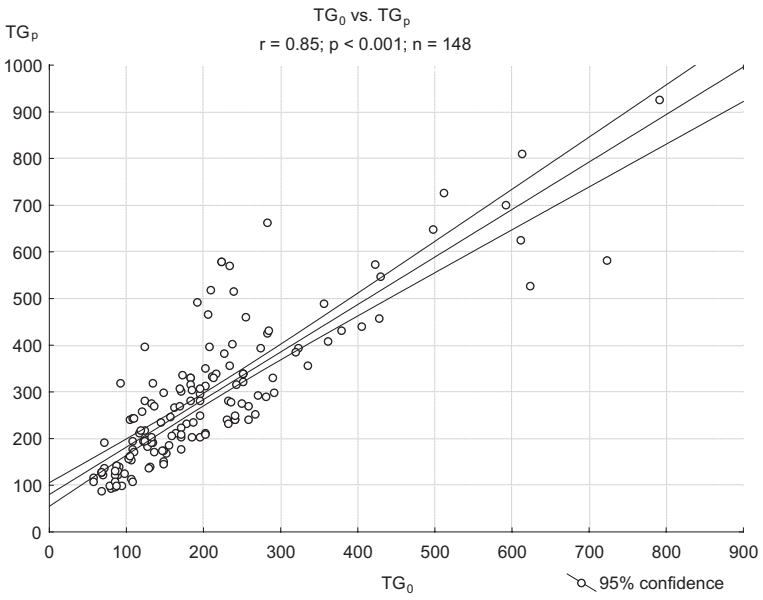

Fig. 2. Linear correlation between fasting (TG_o) and postprandial (TG_p) TG before treatment in the whole study group of 148 men

Ryc. 2. Liniowa zależność między TG na czczo (TG_0) i TG po posiłku (TG_p) przed leczeniem w całej grupie 148 mężczyzn

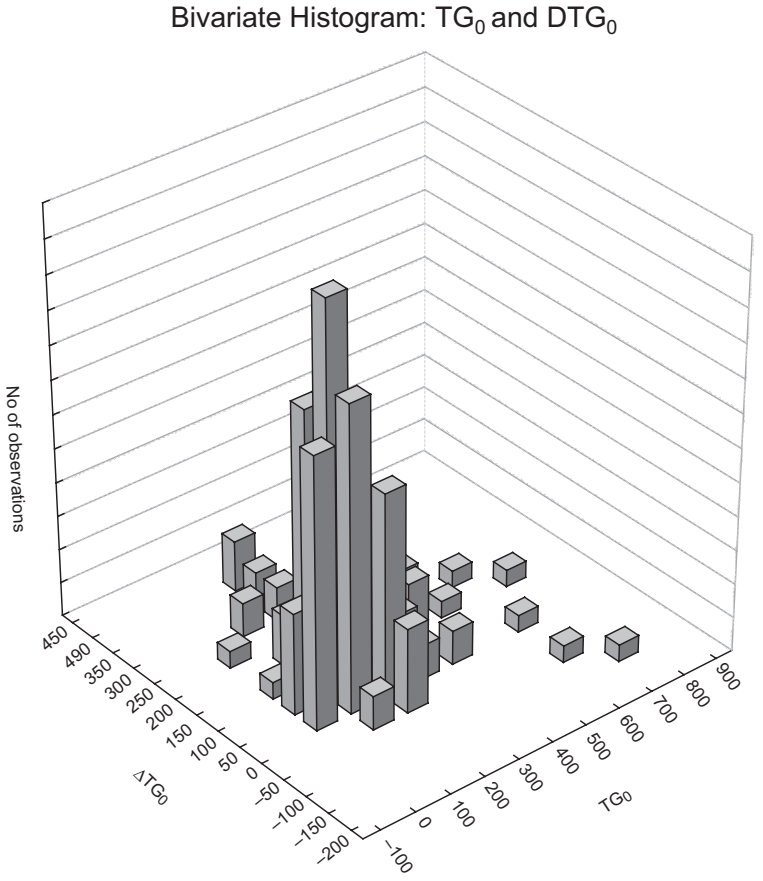

Fig. 3. Distribution of TG_o and ΔTG in the whole study group of 148 men at the beginning of the study

Ryc. 3. Rozmieszczenie zmiennych: TG_O i ΔTG w całej grupie 148 mężczyzn na początku badania

On the other hand, the anti-inflammatory action of fenofibrate mediated by a decrease in TG and increase in HDL is well documented. An inhibitory effect of fenofibrate on the production of inflammatory cytokines and hepatic-synthesized inflammatory proteins was also shown [38, 39].

In this study, positive correlation between fasting TG and hs-CRP coexisting with a negative correlation between fasting HDL_3-C and hs-CRP was shown only in the group of normolipemic men. This coexistence can be due to the inverse relationship between fasting TG and HDL_3-C; however, it is consistent with the pro-inflammatory effect of TG-rich lipoprotein and the anti-inflammatory effect of HDL [8, 34]. Interestingly, there was no correlation between TG and hs-CRP or between HDL_3-C and hs-CRP in the men with hypertriglyceridemia, and treatment with fibrate

did not restore them. Instead, the link between HDL_3-C and hs-CRP existed postprandially (before pharmacotherapy) and appeared in the fasted state (during treatment) in the men with hypercholesterolemia (Table 4). Another inflammatory mechanism induced by postprandial lipemia, i.e. activation of the complement system, was shown similarly in healthy subjects and in patients with hypercholesterolemia [8]. The HDL_3 subfraction possibly participates in the inflammatory response of vessel walls and its role seems to be protective. The inverse relationship between postprandial HDL_3 and hs-CRP in healthy men and patients with hypercholesterolemia confirms this hypothesis.

Of course, the present study has the limitation of being a relatively small one on well-selected patients, the inclusion of men only, and the relatively narrow age range. However, the use of standardized meals in hyper- and normolipemic men points out disturbances in the lipid homeostasis system in hyperlipemic men. The abnormally high postprandial triglyceridemia indicates impaired system efficiency. It is interesting that the physiological correlations between apo B and LDL-cholesterol, apo A and HDL-cholesterol, and TG and HDL-cholesterol were restored by hypolipemic pharmacotherapy.

The authors concluded that increased postprandial lipemia in hyperlipemic men was associated with increased inflammatory activity and HDL_3-cholesterol seems to have anti-inflammatory properties. Hypolipemic therapy decreased postprandial lipemia and at least partially recovered the regulatory function in lipid homeostasis.

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