Adipose tissue activity in relation to overweight or obesity

Aktywność tkanki tłuszczowej w powiązaniu z nadwagą i otyłością

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Abstract

Introduction: Obesity is associated with a number of diseases resulting from the excessive amount of adipose tissue. The aim of this study was to investigate the correlation between the quantity of adipose tissue and the prevalence of metabolic disturbances, and the concentration of adipokines and proinflammatory cytokines in obese or overweight patients.

Material and methods: Fifty-five middle-aged subjects with body mass index (BMI) > 25 kg/m^2 took part in this study. Twenty-three healthy people with normal BMI formed the control group. Twenty-one people from the study group were on a low-calorie diet. All subjects underwent anthropometric assessment, laboratory investigations, and blood-pressure examination.

Results: Patients with obesity or overweight, in comparison to those with normal BMI, showed insulin resistance and a higher concentration of high sensitivity C-reactive protein (hs-CRP), plasminogen activator inhibitor 1 (PAI-1), and interleukin 6 (Il-6). The concentration of adiponectin was significantly lower in this group.
The patients on the low-calorie diet had significantly lower concentrations of leptin when compared to other obese people; moreover, a trend towards decreased hs-CRP concentration was seen.
A significant positive correlation between leptin and hs-CRP was observed. The serum concentration of adiponectin was inversely correlated with that of TNF-α, IL-6, hs-CRP, and PAI-1.

Conclusions: The results of this study may suggest the beneficial impact of a low-calorie diet on the slowing down of inflammatory processes. The observed negative correlation between the concentrations of adiponectin and inflammatory cytokines may confirm the anti-inflammatory activity of this adipokine. **(Pol J Endocrinol 2010; 61 (2): 160–168)**

Key words: *obesity, adipokines, inflammation*

Streszczenie

Wstęp: Otyłość wiąże się z nadmiernym gromadzeniem tkanki tłuszczowej i w konsekwencji prowadzi do wielu poważnych stanów chorobowych. Celem pracy było zbadanie związku pomiędzy ilością tkanki tłuszczowej a występowaniem powikłań metabolicznych, stężeniem adipokin oraz cytokin prozapalnych u osób z nadwagą lub otyłością.

Materiał i metody: W badaniu wzięło udział 55 osób w średnim wieku ze wskaźnikiem masy ciała (BMI, *body mass index*) poniżej 25 kg/m^2. Grupę kontrolną stanowiły 23 zdrowe osoby z BMI w granicach normy. Dietę niskokaloryczną stosowało 21 osób spośród grupy badanej. U wszystkich osób wykonano pomiary antropometryczne, badania biochemiczne oraz pomiar ciśnienia tętniczego.

Wyniki: U pacjentów z nadwagą lub otyłością stwierdzono cechy insulinooporności, podwyższone stężenia wysoko czułego białka C-reaktywnego (hs-CRP, *high sensitivity C-reactive protein*), inhibitora aktywatora plasminogenu 1 (PAI-1, *plasminogen activator inhibitor 1*) oraz interleukiny 6 (IL-6, *interleukin 6*) w porównaniu z osobami z prawidłową masą ciała. Stężenie adiponektyny było znacząco niższe w grupie z nadwagą i otyłością.
Otyli pacjenci stosujący dietę niskokaloryczną mieli znacząco niższe stężenia leptyny oraz wykazywali tendencję do niższych wartości hs-CRP, w porównaniu z pozostałymi osobami z nadwagą lub otyłością. W badanu stwierdzono dodatnią korelację pomiędzy stężeniem leptyny i hs-CRP, natomiast stężenie adiponektyny ujemnie korelowało z TNF-α, IL-6, hs-CRP oraz PAI-1.

Wnioski: Uzyskane wyniki sugerują pozytywny wpływ zastosowania diety niskokalorycznej na zmniejszenie przewlekłego stanu zapalnego u osób z nadwagą czy otyłością. Obserwowana ujemna korelacja pomiędzy adiponektyną a cytokinami prozaplanymi potwierdza jej przeciwzapalane właściwości.
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Słowa kluczowe: *otyłość, adipokiny, stan zapalny*

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Introduction

Obesity is a chronic disease that concerns over a billion adult people throughout the world. It is estimated that the number of those affected by the disease will double by the year 2030. Consequently, we can talk about an obesity epidemic which is going to become the biggest health problem of our century. What is more, along with the number of those suffering from obesity, the prevalence of complications resulting from the excess of adipose tissue is also growing [1–3]

Adipose tissue is the biggest energy reservoir of the organism. The main function of adipose tissue is synthesis and storage of triglycerides in the period of positive energy balance. It is involved in the mobilization of stored energy in the period of negative energy balance.

Adipose tissue plays a role as a mechanical shield for tissues lying in deeper parts as well as a thermal isolator [4–6].

Moreover, adipose tissue is the location of synthesis of numerous, metabolically active proteins, the so-called adipokines. These proteins play an important role in the regulation of local and systemic metabolism, showing typical endocrine activity. That is to say, adipose tissue is a significant element of the endocrine system in humans [4, 6–8].

Adipokines are responsible for the interactions between adipose tissue, muscular tissue, adrenal cortex, and the central and sympathetic nervous system. They take part in maintaining energetic balance, and they have an influence on insulin sensitivity, blood pressure regulation, immunological processes, angiogenesis, fat metabolism, and haemostasis [4, 8–11]. Ghrelin, the only orexigenic peptide produced by the digestive tract, is reduced in obesity. Together with adipokines, ghrelin modulates appetite and energy balance in obese patients [12].

Adipose tissue is the place of synthesis for many proteins involved in inflammatory processes. Cytokines connected with inflammation and secreted by adipocyte include, among others, TNF-α, numerous interleukins (IL-1β, IL-6, IL-8, IL-10), plasminogen activator inhibitor 1 (PAI-1), monocyte chemotactic protein 1 (MCP-1), and macrophage migration inhibitory factor (MIF) [13].

Adipokines such as leptin, resistin, Vascular Endothelial Growth Factor (VEGF), and Nerve Growth Factor (NGF) are also related to the development of inflammation. The concentration of most pro-inflammatory cytokines (which are produced more by macrophages than by adipocytes) increases along with the growth of fat body mass.

Therefore, obesity may be characterized by a co-existing chronic inflammatory state. A positive correlation between the body mass index (BMI) and CRP values has been described. Increased CRP levels are observed in patients with metabolic syndrome and insulin resistance [14]. In addition, CRP concentration negatively correlates with adiponectin levels. Chronic inflammation may play a leading role in the development of insulin resistance and metabolic syndrome [6, 9, 15–17].

Thus, obesity is related to disordered, inadequate immune reaction and higher risk of diseases such as diabetes and atherosclerosis.

Balanced nutrition is the only way of maintaining proper function of the immune system. The ongoing inflammatory process in adipose tissue is similar in mechanism to the inflammatory reaction present in malignant and autoimmune diseases [18].

Nowadays it is assumed that unfavourable changes in secretion of adipose tissue hormones and inflammatory cytokines caused by obesity have an influence the development of metabolic syndrome and vascular complications. Since the discovery of leptin and the other adipokines, studies on the aetiology of diseases related to obesity have been aimed at the understanding of metabolic and endocrine functions of the adipose tissue [11, 17].

The aim of this study was to investigate the correlation between the amount of adipose tissue and the prevalence of metabolic disturbances as well as the concentrations of adipokines and proinflammatory cytokines in obese or overweight patients.

Material and methods

The study was performed in a group of 55 patients with obesity or overweight (called the overweight group). The group was made up of adult subjects (38 women and 17 men) with BMI over 25 kg/m². All patients were stable, without clinical signs of acute inflammation.

They started treatment in the Out-Patients' Ambulatory of the Clinical Nutrition Department of the Medical University of Gdansk. The basic criteria of inclusion to the study were:
— BMI > 25 kg/m²;
— age > 18 years

The patients were interviewed regading their lifestyle and diet. No specific standard diet was given to the patients in this study, with the exception 21 patients on a low-calorie diet for one month. In the group of 21 patients, 10 had moderate physical activity. They were introduced to an exercise program of 1 hour of jogging twice a week in a gymnasium.

Patients thought to have secondary obesity as judged by interviews and examinations were excluded from the study. Also, women taking oral contraceptives or hormonal replacement therapy, within six months of giving birth or breastfeeding, and patients with endocrine, mental, malignant, or serious medical diseases were excluded.

The control group consisted of 23 healthy people (volunteers) with BMI below 25 kg/m^2 (17 women and 6 men).

The patients underwent anthropometric measurements, laboratory investigations, and blood-pressure examination.

The protocols were approved by the Local Ethics Committee, and informed consent was obtained from each patient.

Anthropometric measurements

The following measurements were determined:
— body mass (kg), waist circumference (cm), hip circumference (cm);
— BMI — was calculated as the ratio of the current body mass/height^2 [kg/m^2]. BMI values in the range of 25–30 kg/m^2 were termed overweight, BMI ≥ 30 kg/m^2 was called obesity [3];
— WHR — estimated based on waist to hip circumferences ratio;
— body composition: the body fat content (%F) and lean body mass (LBM) were obtained by near- infrared spectroscopy method (NIR) using a Futrex 5000A unit (Gatesburg Inc., USA).

Body mass and height were measured with attested electronic scales and a body-height measuring device.

Laboratory assay

Blood samples were collected after an overnight fast of 12 hours and the levels of the following compounds were measured in serum:
— Glucose by enzymatic-calorimetric method, EMAPOL;
— Insulin by MEIA method (microparticle enzyme immunoassay), using units and IMX by Abbott, USA;
— Leptin by ELISA method, DRG Germany units and read on STAT FAX 2200, USA;
— Adiponectin by ELISA method, Linco (USA);
— Resistin by ELISA method, Linco (USA);
— TNF-alpha by ELISA method, Bender MedSystem (Austria);
— hs-CRP DRG (Germany);
— IL-6 Bender MedSystem (Austria);
— PAI-1 by ELISA method, Roche (France);
— total cholesterol (TC), triglycerides (TG), HDL-cholesterol (HDL) by routine methods using a Hitachi 911.

Insulin-resistance HOMA1-IR index was calculated according to the following formula: fasting insulin level (mU/L) × fasting glucose level (mmol/L) / 22.5.

Blood pressure was checked twice: sitting and after at least 15 minutes' rest using a proper sleeve. In this study an average from the two measurements is given.

Statistical analysis

The data are expressed as means ± SD (statistical deviation). Significant differences were defined as p < 0.05. The correlations and significance were evaluated with nonparametric statistics. Logistic regression method was also used (using "Statistica version 7.1"; StatSoft, Polska, Kraków, 2005).

Results

The characteristics of the studied groups are shown in Table I. The mean age of the patients was 38.8 ± 10.2 years in the overweight group and 36.3 ± 9.1 years in the control group. There was no significant difference in the age and sex of subjects between the control and overweight groups. Among the investigated population, 21 patients were on a low-calorie (LC) diet (1200––1800 kcal/daily), and 10 of these patients took part in physical activities at the same time.

In the study group, six people (10.9%) were treated for high blood pressure. Moreover, five patients in the study group had abnormal fasting glucose levels (treated non pharmacologically). None of the patients was treated for dyslipidaemia.

In the study group, the mean BMI was 33.8 kg/m^2, mean%F — 41%, and waist circumference — 107.9 cm. In the control group, the mean BMI was 22.2 kg/m^2,%F — 26.3%, and waist circumference 76.9 cm.

Both groups differed in all studied anthropometrical parameters with the exception of height. Additionally, SBP (systolic blood pressure) and DBP (diastolic blood pressure) were significantly higher in the overweight group when compared to the control group (see Table I).

Insulin resistance levels in both groups are shown in Table I.

In the overweight group the mean concentration of insulin was higher than in the control group (22.8 ± ± 17.2 μIU/mL v. 10.1 ± 2.9 μIU/mL).

In the overweight group a wide dispersion of results was observed: the range of insulin concentration was between 5.5 and 89.0 μIU/mL.

Mean value of HOMA index in the overweight group was 5.2 ± 4 compared to 2.4 ± 0.7 in the controls. The differences in the parameters of insulin resistance were statistically significant (see Table I).

Mean concentrations of fasting glucose in the overweight group and control group were similar. Both groups differed with regard to all lipid parameters.

What is more, there were statistically significant differences in the mean concentrations of hs-CRP and PAI-1 (see Table II). The positive correlation between hs-CRP and BMI are shown in Figure 1.

Table I. *The anthropometric measurements, SBP, DBP, and markers of insulin resistance in both studied groups*

Tabela I. Pomiary antropometryczne, skurczowe ciśnienie tętnicze, rozkurczowe ciśniene tętnicze i markery insulino-oporności w obu grupach badanych

Parameters	Overweight (n = 55)	Control (n = 23)	p
F/M	38/17	17/6	ns
Age (years) Mean ± SD Range	38.8 ± 10.2 19–59	36.3 ± 9.10 28–55	ns
Height [cm] Mean ± SD Range	168.7 ± 9.9 152–200	168.8 ± 7.2 155–185	ns
Body weight [kg] Mean ± SD Range	96.6 ± 21.2 65.5–150	63.2 ± 7.8 48.5–78	< 0.001
BMI [kg/m²] Mean ± SD Range	33.8 ± 6.1 26–50.7	22.2 ± 1.9 18.6–24.7	< 0.001
Waist circumference [cm] Mean ± SD Range	107.9 ± 15.2 88–165	76.9 ± 6.9 64–93	< 0.001
Hip circumference [cm] Mean ± SD Range	105 ± 10.4 91–150	97.3 ± 5.9 88–109	< 0.001
WHR Mean ± SD Range	0.94 ± 0.08 0.8–1.14	0.79 ± 0.07 0.7–0.93	< 0.001
Body fat (%) Mean ± SD Range	41.5 ± 7.4 25–60	26.3 ± 5.0 16.8–34.5	< 0.001
Body fat [kg] Mean ± SD Range	40.8 ± 14.1 21.2–80.7	16.7 ± 3.8 9.4–22.8	< 0.001
SBP [mm Hg] Mean ± SD Range	128.3 ± 17.8 100–170	101.7 ± 10.4 90–127.5	< 0.001
DBP [mm Hg] Mean ± SD Range	81.1 ± 12.2 60–100	67.3 ± 6.9 60–80	< 0.001
Insulin [ìIU/mL] Mean ± SD Range	22.8 ± 17.2 5.5–89	10.1 ± 2.9 6.8–17.2	< 0.001
HOMA Mean ± SD Range	5.2 ± 4.0 1.0–21.3	2.4 ± 0.74 1.2–3.9	< 0.001
Glucose [mg/dL] Mean ± SD Range	90.7 ± 10.8 74–133	86.6 ± 8.8 69.6–98	ns

The mean concentration of adiponectin in the overweight group was 16.7 μg/mL and IL-6 level was 3.0 pg//mL. In the control group, the mean concentration of adiponectin was higher (24.2 μg/mL), while IL-6 was lower (2.5 pg/mL). The differences were statistically significant (Table II, Fig. 2).

Table II. *The biochemical parameters in both studied groups*

Tabela II. *Parametry biochemiczne w obu badanych grupach*

Parameter	Overweight (n = 55)	Control (n = 23)	p
hs-CRP [mg/L] Mean ± SD Range	7.9 ± 3.9 1.0–10.65	4.8 ± 3.4 1.2–13.3	0.002
PAI-1 [ng/mL]* Mean ± SD Range	61.9 ± 30.2 21.2–145.2	21.8 ± 13.4 5.9–56.7	< 0.001
Total cholesterol [mg/dL] Mean ± SD Range	220.7 ± 50.6 152–452	196.3 ± 35.2 131–273	0.04
LDL [mg/dL] Mean ± SD Range	140.6 ± 44.8 66.1–358.6	109.2 ± 29.7 53–187.2	0.04
HDL [mg/dL] Mean ± SD Range	45.3 ± 10.1 27.4–70	57.4 ± 17.4 30.8–99.4	0.003
Triglycerides [mg/dL] Mean ± SD Range	170.8 ± 95.3 37–457	99 ± 45.7 52–225	< 0.001
Adiponectin [ìg/mL] Mean ± SD Range	16.7 ± 9.1 3.1–46.7	24.2 ± 8.6 12–49.1	< 0.001
Resistin [ng/mL] Mean ± SD Range	25 ± 16.2 2.2–70.5	23.2 ± 15.4 9.2–83.8	ns
Leptin [ng/mL] Mean ± SD Range	8.1 ± 10.7 0.5–40.5	6.6 ± 10.9 0.5–38.5	ns
TNF-α [pg/mL] Mean ± SD Range	16.7 ± 10.7 5–66	14.3 ± 8.6 4–32	ns
Interleukin 6 [pg/mL] Mean ± SD Range	3.0 ± 0.8 1.8–6.0	2.5 ± 0.4 1.6–3.4	0.03

*for PAI-1 in the obese group : n = 25, in the control group n = 15

The difference between the mean levels of resistin, TNF-α, and leptin in both studied groups was not statistically significant. However, the concentration of leptin in the overweight group was almost 20%, and TNF-α was about 15% higher in comparison to the controls (Table II).

The univariate analysis demonstrated a significant negative correlation between the concentrations of adiponectin and BMI, WHR, waist circumference, %F, insulin concentration, and HOMA-IR values (see Table III). Adiponectin correlated positively with HDL-cholesterol, negatively with LDL–cholesterol, and negatively with the concentration of triglycerides (see Table IV). Moreover, adiponectin showed a negative correlation with TNF-α, IL-6, hs-CRP, and PAI-1 (see Table V).
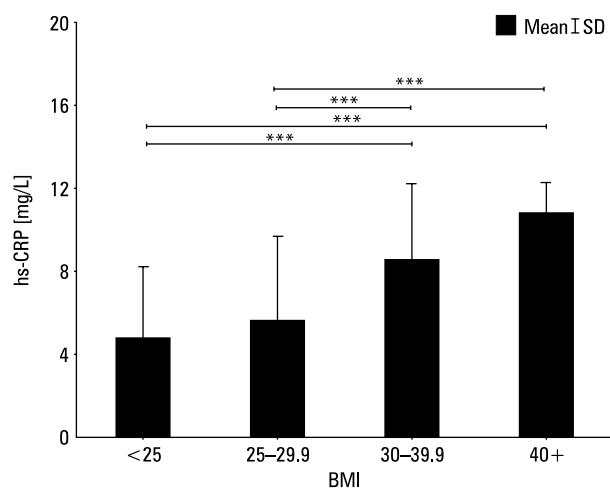
Figure 1. *Mean plasma levels of hs-CRP in relation to BMI.*
***$p \leq 0.001$*
Rycina 1. *Średnie stężenie hs-CRP w osoczu w zależności od BMI.*
***$p \leq 0,001$*
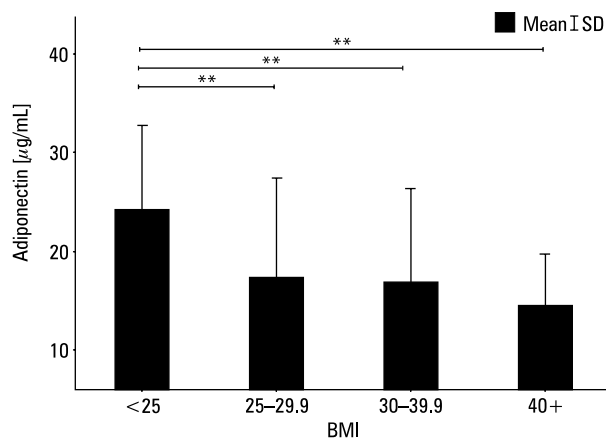
Figure 2. *The mean levels of adiponectin in relation to BMI.*
** $p \leq 0.01$
Rycina 2. *Średnie stężenie adiponektyny w zależności od BMI.*
** $p \leq 0,001$

A significant negative correlation was also observed between adiponectin and SBP as well as DBP (p < 0.001 for both variables).

Leptin concentration correlated positively with hs-CRP (see Table V).

Patients on the LC diet

Patients on the LC diet presented a significantly lower mean leptin concentration when compared to other obese people (0.9 mg/mL *v.* 12.5 mg/mL, p < 0.001) (Fig. 3).

What is more, hs-CRP concentration was lower in patients on LC diet than in other patients (6.2 mg/L *v.* 8.6 mg/L). This difference was close to being of statistical significance (p = 0.08).

Concentrations of other adipokines were not statistically significantly affected by the LC diet. Adiponectin concentrations in woman were significantly higher than in men (21.3 ± 9.7 *v.* 13 ± 6.2 μg/mL (p < 0.001), respectively). No significant difference in the concentration of resistin and leptin was observed between the two genders.

Discussion

Patients in the overweight group had levels of insulin and insulin resistance two-times higher compared with the controls. Hyperinsulinaemia and increased insulin resistance, as demonstrated by HOMA index, in persons with an excessive amount of adipose tissue were confirmed in numerous observations [19–27].

Blum et al. [28] observed differences in HOMA index value even in a small studied group with moderate obesity. Insulin resistance is a problem of obese people, which increases with the age of studied patients [29].

Our study population was significantly different from the control group with regard to all lipid parameters. Hyperinsulinaemia and lowered concentration of HDL-cholesterol co-existing with obesity have been described many times [20, 21, 25, 30].

As demonstrated by others authors, the concentration of leptin in obese subjects is higher compared to subjects with normal weight and shows a positive correlation with BMI and WHR [22, 31, 32].

In our study there was no significant difference between leptin concentrations in the overweight group in comparison to the control group. However, there was a significant difference between leptin levels in obese people on the LC diet and the other obese subjects. The participants of the overweight group who were on the LC diet had almost 14-times lower mean leptin concentration when compared to other obese patients. We supposed that the lack of significant differences in mean leptin levels in the overweight and control groups was the result of the LC diet used by 23 patients. Even a short period of low food intake significantly lowers leptin concentrations, disproportionately to body weight reduction [33]. Other investigators noted a significant decrease in the concentration of leptin after just a 24-hour period of starvation, or a decrease of 72% after just 24 hours of calorie restriction [34, 35]. The above results suggest that leptin secretion is also dependent on other factors, not only on the content of body weight or body fat [34].

During reduction of body weight, leptin concentration is significantly lower when compared to during a stable period, and what is more, the effect is not dependent on initial body weight or body composition [36]. The described changes in leptin concentration suggest

Table III. *Correlations between studied parameters in overweight group in univariate analysis*

Tabela III. *Korelacja między badanymi parametrami w grupie pacjentów z nadwagą w analizie jednozmiennowej*

	Insulin [iIU/mL]	HOMA	WHR	Waist circumference [cm]	F (%)	F [kg]	BMI [kg/m²]
Adiponectin	−0.49***	−0.47***	−0.55***	−0.43***	−0.13	−0.29**	−0.35***
Resistin	−0.10	−0.09	−0.19	0.03	0.10	0.14	0.10
Leptin	−0.01	−0.01	−0.02	0.13	0.12	0.17	0.20
TNF-α	0.10	0.12	0.16	0.10	−0.06	0.02	0.06
Interleukin 6	0.19	0.19	0.28*	0.38***	0.31***	0.34***	0.36***
hs-CRP	0.5***	0.48***	0.09	0.35**	0.41***	0.46***	0.49***
PAI-1	0.59***	0.63***	0.52**	0.53***	0.51***	0.54***	0.59***
Cortisol	0.32**	0.32***	0.08	0.26*	0.33***	0.32***	0.35***
Total Cholesterol	0.05	0.07	0.17	0.18	0.29**	0.23*	0.24*
LDL-Cholesterol	0.12	0.13	0.2	0.23*	0.33***	0.28**	0.29**
HDL-Cholesterol	−0.41***	−0.40***	−0.48***	−0.44***	−0.22*	−0.35***	−0.40***
Triglycerides	0.22	0.23*	0.47***	0.44***	0.35***	0.39***	0.41***
Insulin [μIU/mL]	–	–	0.35***	0.51***	0.40***	0.54***	0.56***
HOMA	–	–	0.35***	0.53***	0.39***	0.55***	0.56***

*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001

Table IV. *Correlations between studied biochemical parameters in overweight group in univariate analysis*

Tabela IV. *Korelacja między badanymi parametrami biochemicznymi w grupie pacjentów z nadwaga w analizie jednozmiennowej*

	Total cholesterol	LDL-cholesterol	HDL-cholesterol	Triglycerides
Adiponectin	−0.10	−0.08	0.48***	−0.41***
Resistin	−0.09	−0.01	0.13	−0.23*
Leptin	−0.03	0.00	−0.05	0.01
TNF-α	−0.03	−0.03	−0.19	0.15
IL-6	−0.09	0.06	−0.34***	0.09
hs-CRP	0.05	0.15	−0.20	0.06
PAI-1	0.32*	0.40**	−0.50***	0.46***

*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001

Table V. *Correlations between studied adipokines in overweight group in univariate analysis*

Tabela V. *Korelacja między badanymi adipokinami u pacjentów z nadwagą w analizie jednozmiennowej*

	Adiponectin	Resistin	Leptin	TNF-α	IL-6
Resistin	0.31**	–	–	–	–
Leptin	0.08	0.14	–	–	–
TNF-α	−0.24*	−0.15	0.09	–	–
IL-6	−0.23*	0.05	0.07	0.16	–
hs-CRP	−0.23*	0.18	0.22*	−0.15	0.16
PAI-1	−0.54***	−0.01	−0.20	0.17	0.40**

*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001
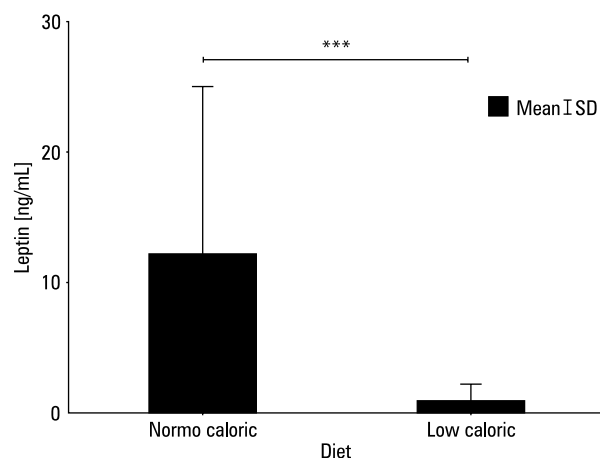
Figure 3. *The plasma leptin levels in relation to diet in the overweight group. *** p ≤ 0.001*

Rycina 3. *Osoczowe stężenie leptyny w zależności od diety w grupie z nadwagą ***p ≤ 0,001*

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that leptin is a sensitive marker of current energy processes [37, 38].

The regulation of leptin gene expression is highly complex as it involves multiple mediators the relative importance of which is, as yet, undetermined. The important regulatory factors are glucocorticoids, insulin, and thyroid hormones. Thyroid hormones inhibit leptin gene expression, and sex steroids such as oestrogen increase leptin mRNA levels. Usually females have significantly higher leptin levels than males [39], this sexual dimorphism was not observed in our study. In our overweight group, the mean age of males was higher than that of the females, and the group of males (< 30% of all studied patients) was relatively small.

The lack of difference in mean leptin concentrations which we observed may also be the result of higher energy expenditure in the studied group. It has been observed that leptin concentrations could be modified by physical activity, regardless of body weight [40, 41]. Some authors have shown that moderate physical activity may support metabolism regulation by decreasing concentrations of leptin and leptin resistance, despite a lack of noticeable change in BMI.

In our study, there was no significant difference of serum resistin and TNF concentrations in the overweight group in comparison to the control group. The previous studies concerning the role of resistin in obesity and insulin resistance were ambiguous. Only a few authors indicated increased resistin concentration or expression of mRNA for resistin in obesity. They presented decreased expression of mRNA for resistin in adipose tissue in obese animals. In addition, in several studies in obese humans there was no visible relation between obesity and resistin level [42].

In obesity and hyperinsulinaemia status, increased expression of mRNA for TNF in adipose tissue was observed [8]. Some previous studies, although not all, showed a positive correlation between expression mRNA in adipose tissue and serum concentration of TNF-α [43].

In the overweight group there a positive correlation between hs-CRP and leptin concentration was observed. This observation confirmed the pro-inflammatory activity of leptin described in literature [16]. Thus, it may be assumed that in obese people (as a result of leptin resistance) there exists a lack of leptin anorexigenic activity. However, there was pro-inflammatory activity of leptin. As we have shown, being on a LC diet allows a significant decrease in leptin concentration. In addition, there was a visible tendency towards lowered hs-CRP concentration on the LC diet. Aksungar et al. [44] also noticed a positive influence of the LC diet on such markers of chronic inflammation as hs-CRP. The reduction in leptin and hs-CRP concentrations is high-

er in the case of a low-carbohydrate diet than of a low-fat diet [45].

Adiponectin is the main product of adipose tissue. An increase in body fat content results in a decrease in adiponectin serum concentration. In our study, overweight subjects had about 1.5-times lower concentrations of this adipokine, which has anti-inflammatory and anti-sclerotic effects. In our study, similarly to studies of other authors [46–52], in the overweight group adiponectin concentration decreased along with increased BMI, WHR,%F, and waist circumference. Also, adiponectin levels decreased along with increased insulin and HOMA index value. Adiponectin concentrations were significantly higher in women [31, 48]. In the overweight group, concentrations of adiponectin correlated positively with HDL-cholesterol and negatively with triglycerides. However, there was no correlation between adiponectin and total cholesterol or LDL fraction.

We observed a negative correlation of adiponectin with SBP and DBP. Thus, along with a lowering of adiponectin concentration, lipid abnormalities typical for the metabolic syndrome as well as higher blood pressure were observed. Such results confirm the correlation between hypoadiponectinaemia and metabolic syndrome [31, 52].

The adiponectin in the overweight group showed a negative correlation with concentrations of pro-inflammatory cytokines IL-6 and TNF-α. Brunn et al. presented data about the influence of this cytokine on adiponectin secretion. They incubated a piece of subcutaneous adipose tissue with IL-6 + IL6-R and with TNF-α. The addition of such cytokines resulted in lowering of mRNA for adiponectin [26]. Other authors also observed lower expression of mRNA for adiponectin while, at the same time, TNF-α in adipose tissue was increasing [49].

TNF-α, which is mostly synthesized by adipose tissue macrophages, inhibits adiponectin transcription in adipocytes. Therefore, it may be supposed that the inflammatory process in adipose tissue areas, which is connected with obesity, is a cause of decreased concentration of adiponectin in obese people [16].

In our study, adiponectin levels negatively correlated to concentrations of hs-CRP and PAI-1. This possibly suggests the anti-inflammatory and anti-coagulant activity of adiponectin [46, 47, 53, 54].

hs-CRP, as well as PAI-1, were significantly higher in the overweight group when compared to control group, similarly to other studies [20, 18, 22, 39]. In our studied population, concentrations of hs-CRP increased along with levels of obesity and insulin resistance. The higher concentrations of IL-6 and hs-CRP which we observed in the overweight group, as well as the positive correlation between inflammatory cytokines and %F,

may confirm the hypothesis that obesity is connected to subclinical, chronic inflammation. The inflammatory process co-existing with obesity is, among others, the result of infiltration of adipose tissue by macrophages. They may form up to 50% of cells of adipose tissue. Their number grows along with accumulation of adipose tissue and size of adipocytes. Adipose tissue macrophages have receptors for both dominating adipokines: leptin and adiponectin [15].

Adiponectin induces apoptosis of monocytes and inhibits the process of phagocytosis by macrophages. Leptin acts in the opposite way: it increases proliferation and migration of monocytes and stimulates phagocytosis. Thus, the inflammatory reaction may be supported by abnormal auto- and paracrine activity of adipose tissue. Subclinical inflammation probably plays the most important role in the development of insulin resistance and type 2 diabetes in obese patients [16]. The leptin-adiponectin ratio is regarded as a potential atherogenic index in obese patients [55].

Conclusions

1. The results show the significant role of non-pharmacological procedure in obesity treatment and the positive results of introducing the treatment as early as possible. The earlier the implementation of a LC diet, the better the chances for regression of the metabolic disturbances.
2. One of the mechanisms through which a low-calorie diet may limit the development of the inflammatory process related to obesity could be the decrease in leptin concentration.
3. The decrease in adiponectin concentration, which is proportional to the level of insulin resistance and obesity, may be one of the causes of pro-inflammatory and pro-coagulation trends in overweight and obese people.

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