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# „Cytokine and adipokine concentration and lifestyle, body mass composition, resting metabolism in obese people”

PhD Thesis - Abstract

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The prevalence of obesity and overweight in developed countries has become a serious health and social problem. The World Health Organization collected statistics from 1975 to 2016. The prevalence of obesity in Poland increased from 10.7% to 23.1%. In the world in 2016 among adults as much as 39% were overweight (BMI ≥ 25 kg/m2), and 11% of men and 15% of women were obese (BMI ≥30 kg/m2). This gives 2 billion overweight people and over half a billion obese people. It is even suggested that in 2030 overweight and obesity will reach 89% and 85% in men and women respectively.

Excess body fat is the result of consuming too many calories compared to the body's energy requirements. The causes of excess food consumption differ, e.g.: changes in food quality, industrialisation, lack of exercise due to more frequent use of means of transport and sedentary lifestyle, low amount of sleep, genes, pre- and perinatal factors, physical and social health, medication consumption and low level of education.

Abnormal body weight in middle age reduces life expectancy by 4-7 years. Additionally, excess body fat increases the possibility of such diseases as insulin resistance, type 2 diabetes, hypertension, heart disease, dyslipidemia. As the amount of adipose tissue increases, so does the incidence of cancer and the risk of complications after trauma and surgery. Excessive adipose tissue also prolongs the time of hospitalization and convalescence, which is associated with higher health care expenses.

The aim of the study was to determine the relationship between diet, lifestyle, body mass composition, resting metabolism and the concentration of mediators associated with inflammation (interleukins: IL-1, IL-6, IL-17A, IL-17F, IL-17C, IL-21, IL-22, IL-23, IFN-γ, TNF-α) and obesity (ghrelin, adiponectin, resistin, leptin, glucose, glucagon, insulin).

Material and methods: The study included a group of adult patients with BMI ≥ 30 kg/m2 (obesity according to WHO classification). 84 people, i.e. 62 women, 22 men, aged from 18 to 74 years were subjected to examinations . Patients came in the morning (from 7:00 a.m. to 10:00 a.m.) to the Natural and Medical Centre for Innovative Research at the Medical Faculty of the University of Rzeszów in order to conduct anthropometric, questionnaire and laboratory tests. The condition to perform the tests was fasting, after more than 24 hours of abstinence from stimulants, diuretics and physical exertion. Pregnant women, people with pacemakers or prostheses, unable to maintain an upright posture, patients with epilepsy, cancer and chronic inflammation were disqualified from the tests. The study group rejected persons taking steroids, antidiabetic (metformin), anti-inflammatory drugs, statins and undergoing insulin therapy.

The blood was collected, centrifuged and frozen. Then, after completion of the tests with commercial kits using the Luminex method, the following were determined: IL-1, IL-6, IL-

17A, IL-17E, IL-17F, IL-21, IL-22, IL-23, IFN-γ, TNF-α as well as ghrelin, adiponectin, resistin, leptin, glucagon and insulin. Growth was measured twice, and the result was averaged for each test subject. Then, each of the subjects was analyzed by means of non-invasive electrical bioimpedance method with a medical examiner. Calorimetry was performed in the morning. In order to minimize the impact of stress, the room in which the test was performed provided ambient temperature and calmness (maximum two people, possibility to cover with a blanket, relaxing music, mild light). The device used to measure the resting metabolism was an indirect calorimeter, also certified by a medical doctor. The measurement took 15 minutes. The respondents also completed a questionnaire related to the lifestyle and frequency of consumption of particular groups of foods with special emphasis on the factors influencing inflammation. Each participant was supposed to complete a dietary logbook covering 3 days (2 working days, 1 weekend) of customary nutrition before enrolling in the study. The method of completing the logbook was explained in detail to all subjects and had to include hours and composition of meals, taking into account the weight or measures of home products and the method of processing. Statistical analysis of the collected material was carried out in the Statistica 13.1 package by StatSoft.

Results: The minimum body weight among the subjects was 70.6 kg, the maximum was 156.4 kg, the average body weight was 103.01 ± 18.23 kg. The subjects measured from 149 to 192 cm of height (average 167.44 ± 9.01 cm). The minimum BMI among the subjects was 30.0 kg/m2 and the maximum was 58.1 kg/m2. The average BMI of the group is 36.65 ± 5.27 kg/m2 . The subjects with obesity of the 1st and 2nd degree were equally 34 persons in each category (40.5%), while 16 persons were suffering from obesity of the 3rd degree 16 (19.0%).

Health condition, drugs and supplements: In the group 25% had hypertension, 3% had fatty liver, 2% had atherosclerosis and 6% had hypothyroidism. Patients who suffered from atherosclerosis had elevated levels of interleukins such as IL-6, IL-1β, IL-17F, IL-23 and adiponectins, patients with hypothyroidism taking levothyroxine had elevated values of IL-1β and TNF-α. Blood pressure increases with age. In women, it is lower than in men. It increases linearly with the increase of body weight as well as with the content of visceral fat, fat-free tissue and muscle mass. Additional factors influencing RR are nutrients contained in dairy products such as lactose, calcium and vitamin B2 and thyroid regulators such as selenium and iodine. Occasional use of NSAIDs causes a decrease in adiponectin levels.

Analysis of body composition: Body weight and its composition affected adipokine and cytokine levels. BMI positively correlated with adiponectin, resistin, leptin, IL-17E, IL-17F, IL 21. Subcutaneous fat tissue was associated with increased amounts of IL-6, IL-17F, insulin,

leptin and resistin. The level of visceral adipose tissue was negatively correlated with the level of ghrelin in the body. The adiponectin value was inversely correlated with the amount of fat-free tissue (muscle, water, bone mass) in the segment (limbs).

Lifestyle: Statistically significant was the relationship between blood glucose level and the amount of fiber, magnesium, potassium, vitamin C consumed, which may result from the large amount of fruit consumed by the respondents. This was confirmed by the results of own research related to the frequency of consumption of individual products. The level of insulin is lower in the respondents, who consume more cholesterol and vitamin D, which is connected with higher consumption of eggs. Additionally, the consumption of milk sugar, so called galactose, is negatively connected with insulin and glucagon levels. The level of blood glucagon decreases with the higher frequency of consumption of potatoes, red meat, milk and eggs. The consumption of protein sources such as fish and red meat and frequent tea lowers the level of ghrelin. The consumption of sour milk products reduces leptin levels in the body. In addition, a high proportion of vitamin D3 in the diet as well as iodine reduce the level of leptin in the serum. Persons supplementing vitamin D3 had lower levels of adiponectin, while its high level positively correlated with high glycemic index of food, alcohol consumption and physical exercise. The value of resistin shows a negative correlation with the frequency of alcohol consumption, positive with the amount of white pasta and red meat consumed. Large amounts of amino acids with anti-inflammatory properties, such as arginine, allanine and glycine, consumed reduce the level of IL-1β in the serum. On the other hand, a higher intake of maltose, a component of glucose-fructose syrup, was correlated with high levels of IL-1β. Higher levels of IL-22 are found in people consuming lysine and tyrosine (animal protein components). Frequent intake of beta-crotene and iodine increases the level of IL-22 in blood. Large amounts of sucrose and galactose were conducive to an increase of TNF-α. With the increase of PRAL ratio of the diet of the subjects, the level of IL-17E increased. High intake of potassium, iron, vitamin B6, vitamin C and folic acid had a supressive effect on IL-17F level. There was a negative relationship between the amount of IL-23 in serum and glycemic index (positive with complex carbohydrates) and alcohol consumption. Frequency of consumption of particular food groups modified the immune response affecting cytokine levels. Consumption of sugar and fruit milk products (rich in sugar or F-G syrup) favoured an increase in IL-6 levels. IL 17A level has a positive correlation with inflammatory supportive confectionery and negative correlation with healthy food products such as vegetables, groats and eggs. The IL-17F level in the blood of the subjects was suppressed by the frequent consumption of red meat. The IL-17F level in blood, increased with the consumption of confectionery and breakfast cereals in large quantities. The

level of IL-17E increased the frequent consumption of fast-food. Lifestyle including physical activity and stimulants have a large influence on the level of interleukins in the blood serum. Physical activity increases the level of IL-6 and decreases the level of IL-22. Cigarette smoking also negatively correlates with the level of IL-22. Consumption of alcohol in an already existing inflammation (e.g. low grade inflammation in obese people) reduces the amount of IL-6, IL-22, IL-23, IL-17E, IL-17F.

Calorimetry results: There was a negative correlation between adiponectin level and resting metabolism measured by calorimetry and a positive correlation between insulin and RMR. The vital capacity was negatively affected by the level of IL-1β, TNF-α, and blood pressure. There was a negative correlation between oxygen consumption and adiponectin levels. There was a negative correlation between the amount of IL-1β, TNF-α in the serum and the frequency of breathing and the percentage of CO2 in the exhaled air. Negative correlation appeared between leptin and resistin levels and VO2/kg. High arterial pressure was associated with higher air capacity per unit of time.