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Epidemiology and pathogenesis of obesity

Epidemiologia i patogeneza otyłości

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S u m m a r y

Obesity is a current health problem reaching the range of the world epidemic. This article reviews the data and literature on epidemiology and the complex pathogenesis of the issue. In addition to health consequences and shortening the life expectancy, obesity is also a growing socio-economic issue.

S t r e s z c z e n i e

Otyłość jest aktualnym problemem zdrowotnym osiągającym skalę epidemii światowej. Niniejsza praca stanowi przegląd danych i piśmiennictwa na temat epidemiologii i złożonej patogenezy zagadnienia. Oprócz konsekwencji zdrowotnych i skrócenia oczekiwanej długości życia otyłość to także rosnący problem społeczno-ekonomiczny.

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INTRODUCTION

The aim of this study was to draw attention to the issue of obesity, which has been growing for over a dozen years, in particular its epidemiology and pathogenesis. Obesity is a consequence of weight gain due to a positive energy balance, i.e.: the consumption of more calories than the body demands. Excessive fat gain, exceeding human body's physiological needs and adaptation possibilities leads to structural and functional defects of many organs and systems, biochemical and physiological disorders, and as a consequence to shortening the life expectancy. Among the many methods assessing the severity of obesity, the most common and most frequently used is the determination of the body mass index (BMI), which is the quotient of body weight (kg) and height (m) squared. Using this method, we recognize overweight in patients with a BMI between 25 and 29.9 kg/m^2, and obesity with BMI above 30 kg/m^2. Morbid obesity is diagnosed when the patient's BMI is above 40 kg/m^2.

REVIEW

Epidemiology of obesity

Until recently, obesity and overweight have been a problem of developed countries. Currently, this problem concerns developing countries as well as third world countries, and at the same time all socio-economic groups. According to the report of the World Health Organization (WHO) of January 2015, the number of obese people has tripled since 1980 and cur-

rently reaches epidemic proportions. In 2014, more than 1.9 billion of world population over 18 were overweight, which is 39%, among them, 600 million were obese (13% of the population, including 11% of men and 15% of women) (1). The highest percentage of obese people is in the United States, where, according to the World Obesity Federation report from 2015, over 60% of adults are overweight and over half of them are obese (2). In Europe, approximately 150 million adults (20% of the population) and 15 million children and adolescents (10% of the population) suffer from obesity. In Poland in 2014, 56.7% of women and 65.8% of men were overweight, and 26.7% of women and 23.5% of men were obese. The obesity problem in Poland has been analyzed within the projects of Pol-MONICA, NATPOL PLUS and the Multicultural National Population Health Survey (WOBASZ) (3-5). In the Polish population between 20 and 74 years old, the average BMI below 25 kg/m^2 has been found in only 47% of respondents, 34% was overweight and 19% was obese. According to 2009 GUS data, the problem concerned over 61% of men (45% were overweight, 17% obese) and almost 45% of women (30% were overweight and 15% obese) (6). The most disturbing, however, is the fact that in 2013 42 million children under the age of 5 were found overweight or obese. Currently, in Europe, about 20% of children are overweight, and nearly 1/3 of them achieve values of BMI suggesting obesity and it is the most common health problem in children. It is estimated that by 2030 one child in 10 will be obese. Among Polish children, overweight were diagnosed in 9.7% of 13-year-old boys and 3.9% of 13-year-old girls (7, 8). What is more, those children will probably remain obese even after reaching adulthood and will have an increased risk of developing diseases leading to a decrease in the quality and length of their lives. It has been proven that along with the increase in BMI the risk of obesity complications, including early death, increases (9, 10). The World Health Organization warns that obesity is responsible for 10-13% of deaths, and the majority of the population lives in countries where overweight and obesity is the cause of death of a larger percentage of society than malnutrition. Obesity leads to a shortened life expectancy of 5-20 years depending on its severity as well as patient's age, sex and race (11). Patients with obesity are more likely to develop diseases such as type 2 diabetes, arterial hypertension, coronary heart disease, strokes or some cancers (endometrium, ovary, breast, prostate, large intestine) (12, 13). 90% of patients with type 2 diabetes are obese or overweight (14). Long-lasting and, above all, unregulated diabetes leads to a number of changes in the body, especially those of micro- and macroangiopathy, which in turn increases the risk of death, myocardial infarction or stroke (15). Studies show that up to 60% of obese patients also develop fatty liver (16, 17), including up to 55% in the pediatric population (18, 19). Although, approximately 20% of obese patients do not find typical changes in the lipid metabolism, most of them present the symptoms of disorders of lipid metabolism, which is associated with an increased risk of developing cardiovascular disease, including myocardial infarction or ischemic stroke (20). Obesity also increases the risk of pancreatitis, gout, hyperuricemia, sleep apnea syndrome, urolithiasis, in women problems with infertilization and delivery, which is associated not only with hormonal changes (increased estradiol, estriol, testosterone, androstendione) and disorders of ovulation, but also with systemic diseases accompanying obesity. Health-related consequences are less serious but also disturbing (21). Reduced mobility, disturbed perception of one's body may increase the risk of depression or personality disorders. In addition, the social and economic costs of obesity are extremely high. In Europe, they absorb up to 6% of health expenditure, depending on the region (22, 23). It should not be forgotten that obese people are less likely to work professionally due to co-morbidities, and children achieve worse results in learning. Unwanted weight gain is caused by a positive energy balance, i.e. more calories than those consumed by a person. The causes of the epidemic are complex. We call many of them the so-called "Environment favorable to obesity" and include such factors as the structure of society, economic policy, socio-economic development (a greater number of urban residents, driving cars, a sedentary lifestyle at home and at work, consumption of processed food, etc.).

Pathogenesis of obesity

The basic problem are eating habits, which have changed significantly in recent decades: irregularity of meals, their incorrect distribution during the day and a small variety of diet, incorrect proportions between specific groups of products or excessive consumption of certain product groups, especially fats and monosaccharides. In 1961, the daily amount of calories consumed per person was 2,300. In 1998, it increased to 2,800, and in 2015 exceeded 3,000. In addition, the total amount of available food increases, which is accompanied by a decrease in its price. At the same time, the amount of fruit and vegetables consumed decreases. According to the WHO European Office, only 30% of boys and 37% of girls age 13 to 15 eat fruit every day. The second main problem is the continuous decline in physical activity in the population of developed and developing countries, which is supported by the environment in which we live (home, work, school, means of transport). Physical activity of at least two thirds of the European population is not satisfactory and is continuing to decline. WHO recommends moderate physical activity for adults at least 30 minutes a day, children at least 60 minutes a day, and it is estimated that in most cases cars are used in Europe to cover a route of no more than 5 km. In addition to such trivial reasons for weight gain, as mentioned above, it is also important to mention such factors as: genetic, non-genetic biological, pharmacological and psychological. There are

many genetic disease syndromes in which excessive fat accumulation occurs, such as the Prader-Willi syndrome, Turner's syndrome, and von Gierki's disease. In a small percentage of the population, monogenic mutations leading to the development of obesity occur. In the majority, however, the tendency to obesity results rather from the mutation of many genes associated with energy intake with food, the level of basic metabolism, and the activity of enzymes responsible for lipid and carbohydrate metabolism. Non-genetic biological agents also play a huge role in the development of obesity. Endocrine disorders, in which excessive weight gain occurs, are primarily a deficiency of growth hormone, hypothyroidism, alleged hypoparathyroidism, Cushing's syndrome, polycystic ovary syndrome or hyperinsulinism. Also, many medications taken regularly result in weight gain. Those include antidepressants (amitriptyline, doxepin, mirtazapine, mianserin), anxiolytic, neuroleptic (phenothiazine derivatives, olanzapine, risperidone), antiepileptic (valproic acid, carbamazepine), corticosteroids or insulin. The occurrence of obesity is inextricably connected with changes in the neurohormonal balance. Ghrelin is a neuropeptide hormone secreted mainly by the cells of the fundus of the stomach, and in a smaller amount in the initial section of the small intestine, hypothalamus, pituitary gland or pancreas. In the stomach, it is not secreted into the lumen of the digestive tract, only to the blood vessels. Nerve cells containing ghrelin receptors are found in the arcuate nucleus of the hypothalamus, which is responsible for the regulation of appetite. Its concentration increases during starvation, especially just before a meal, and decreases under the influence of food (24, 25). Ghrelin also has a negative correlation with the concentration of glucose and insulin in the blood. In addition, it increases the production of growth hormone, ACTH, cortisol, adrenaline and glucagon acting hyperglycemically. It stimulates hepatic gluconeogenesis and inhibits insulin secretion (26). It also increases the uptake of glucose and triacylglycerols by adipocytes by stimulating lipogenesis. What is more, it reduces the secretion of adiponectin, which reduces the level of triacylglycerols, LDL cholesterol and increases HDL (27). Glucagon-like peptide-1 (GLP-1) belongs to the group of intestinal enteric hormones and is secreted by the L-cells of the final section of the small intestine in response to food intake. It stimulates glucose-dependent insulin secretion, delays gastric emptying, inhibits glucagon secretion and hepatic glucose production (28-30). The YY peptide is secreted in the L-cells of the distal jejunum as well as through the colon and ileum cells in response to the meal being taken. The release of PYY occurs already at the beginning of the meal, even before the food content reaches the intestine, which is probably related to the nervous mechanism. In the next stage, hormone secretion depends on the type of food content and is proportional to its calorie content. Significantly higher postprandial increase in peptide concentration is obtained in the case of fatty food, compared with food with the same calories amount, but protein or carbohydrate. The concentration of PYY increases, reaching a plateau after 1-2 hours after food intake and remains elevated to 6 hours. In the peripheral circulation enzymatic modification of the YY peptide occurs, and because it has the ability to cross the blood-brain barrier, its target is the hypothalamic arcuate, where it plays an important role in the regulation and control of food intake (31). The YY peptide also has its peripheral activity. It participates in the regulation of gastrointestinal peristalsis by inhibiting the secretory function of the stomach and pancreas, delaying gut motility and gastric emptying, which reduces appetite (32). Leptin is a hormone produced mainly in adipose tissue in a quantity proportional to its mass (33). It works by reducing appetite, increasing gluconeogenesis and lipolysis in adipose tissue, which in turn causes an increase in the level of free fatty acids in the blood. In addition, leptin inhibits insulin production and the transport of glucose to adipocytes. In obese people, increased levels of leptin in the blood are detected, but leptin receptors sensitivity is reduced, which results in the fact that patients do not feel full despite the delivery of a large energy charge (34). The development of metabolic complications of obesity in the form of mainly, type 2 diabetes or hypercholesterolemia is associated primarily with the accumulation of visceral fat. Today, fatty tissue is believed to be responsible for homeostasis of the body and is an important metabolic organ. The primary function of adipose tissue, which is probably of key importance in the pathogenesis of insulin resistance, is the ability to store lipids in the form of triglycerides (TG). Free fatty acids, which can not be stored in fat tissue in the form of TG, get into the blood, and then into the skeletal muscles and liver, where they intensify gluconeogenesis and reduce the creatinine clearance. Excess free fatty acids, on the other hand, inhibit the transport of glucose to skeletal muscles, glucose phosphorylation and its oxidation. In addition, in the presence of insulin resistance, macrophages of adipose tissue being a source of pro- and anti-inflammatory cytokines play an important role. C-reactive protein, produced mainly in the liver, was the first described protein indicating inflammation and tissue damage (35, 36). It is believed that obese patients develop a strong correlation between the concentration of C-reactive protein in the blood serum and BMI, furthermore, a decrease in body weight causes a decrease in CRP (37, 38).

CONCLUSIONS

Obesity, although it has reached the scale of the world epidemic, is no longer just a health issue. In addition to the consequences as obvious as the development of biochemical and physiological disorders of the body and shortening the life expectancy, it is also an economic and social problem, which has to be managed not only by well developed countries, but also those developing and with low income.

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