Streszczenie w języku angielskim

Introduction

Epidemiological studies on obesity and overweight indicate that it is a significant and continuously growing problem, reaching the status of a global pandemic. Environmental (acquired), genetic (inherited), psychological, endocrinological, and metabolic factors contribute to the increasing number of individuals with obesity. Currently, the inheritance of predisposition to excessive body weight is considered to have a polygenic nature. It is estimated that genetic factors account for about 30-40% of the risk of obesity. Despite extensive research on the genetic basis of obesity, the main gene/mutation that would directly cause the development of this disease has not been identified yet. One of the factors mentioned is the polymorphism of the stearoyl-CoA desaturase gene (SCD). However, both the function of this gene and the associated mechanism of obesity induction are currently unknown. The role of single nucleotide polymorphisms (SNPs) of the SCD gene, including the impact of SNP alleles, is also emphasized. Therefore, the aim of the study was to estimate the variability of the MT-ATP6 mtDNA gene and the degree of relatedness among patients with different nutritional states (based on BMI) and phenotypes of abdominal fat distribution (TOFI, FOTI). Another objective was to determine the occurrence of different alleles in the SNP rs7849 of the SCD gene in individuals with obesity and normal body weight, as well as the influence of the presence of the C allele on carbohydrate and lipid metabolism parameters in the studied individuals.

Material and methods

The observational study was conducted among 116 individuals (77 females and 39 males). The research protocol was approved by the Bioethics Committee of the Medical University (Approval No. APK.002.407.2020, R-I-002/647/2019, and APK.002.39.2021). All participants provided informed, written consent to participate in the study prior to its commencement. Anthropometric measurements (body weight, height, and BMI in kg/m2) were performed on all participants. Patients were divided into the study group (46 females and 29 males with BMI = 30.0-39.9 kg/m2) and the control group (31 females and 10 males with BMI = 18.5-24.9 kg/m2). Body composition analysis using the bioelectrical impedance method and assessment of subcutaneous and visceral fat were conducted using the BioScan 920-2 device. The following parameters were obtained: total fat mass (kg, %) and non-fat tissue mass (kg). Additionally, subcutaneous (cm2) and visceral (cm2) fat areas at the level of the umbilicus were estimated, and the VAT/SAT ratio was determined. The VAT/SAT ratio (visceral adipose

tissue/subcutaneous adipose tissue) was used to determine the phenotype of abdominal fat distribution (subcutaneous and visceral) as TOFI (thin outside fat inside) or FOTI (fat inside thin outside). To examine gene sequences, oral swabs were collected from the cheeks and palate using sterile swab kits. Isolated DNA was used for PCR reactions, and amplified fragments were subsequently sequenced using the Sanger method. The sequences were aligned and subjected to bioinformatic analyses. Biochemical blood tests (fasting glucose, insulin, total cholesterol, LDL and HDL cholesterol fractions, and triglycerides) were performed at the Laboratory Diagnostic Department of the Medical University in Białystok. Results regarding body composition and biochemical blood markers were analyzed using the Statistica 13.3 software program.

Results

The study group consisted of 75 individuals (46 females and 29 males) with obesity, while the control group comprised 41 individuals (31 females and 10 males) with normal body weight. After sequencing the MT-ATP6 gene mtDNA from all samples, 52 haplotypes were identified. The most common haplotype was H1, represented by 42 participants (29 with obesity and 13 with normal body weight). The second most common haplotype was H6, represented by 13 participants (8 with obesity and 5 with normal body weight). The number of haplotypes in the MT-ATP6 gene in both groups was diverse, and each group had haplotypes unique to them. In the study group, these were haplotypes H3-H5, H7-H13, and H15-H31. In the control group, these were haplotypes H33-H52. The genetic variance values (Fst) calculated from the observed variability of MT-ATP6 were not high (0.0046), indicating very low genetic variability between the groups according to Wright's scale. Despite the low Fst values, the haplotype network revealed up to 102 mutations, with the main haplotypes being the aforementioned H1 and H6. In both groups, the majority of patients represented the TOFI phenotype, while the FOTI phenotype was less represented.

Among the patients, the SNP rs7849 in the SCD gene was detected. The observed heterozygosity for homozygous TT was 0.681034483, and the expected heterozygosity was 0.68489893. For heterozygous TC, the observed heterozygosity was 0.293103448, and the expected heterozygosity was 0.299643282. For homozygous CC, the observed heterozygosity was 0.034482759, and the expected heterozygosity was 0.032773484. In all cases, the differences were not statistically significant, indicating that the examined group of patients was in Hardy-Weinberg equilibrium. Heterozygous patients (TC) were observed in both groups, while homozygous CC patients were only present in the control group (with normal body weight). Both heterozygotes and homozygous CC individuals had lower median values of the

HOMA-IR index, as well as lower median concentrations of glucose, insulin, total cholesterol, LDL cholesterol fractions, and triglycerides, while the median concentration of HDL cholesterol fractions was significantly higher.

Conclusions

It was found that despite the low variability of the MT-ATP6 gene in humans based on nutritional status (BMI), the study group exhibited greater haplotype diversity. Among all study participants, no genetic associations in the MT-ATP6 gene were found for the TOFI and FOTI phenotypes. Among the examined patients, homozygous TT for the rs7849 SNP in the SCD gene were most frequently observed (81.3% of individuals with obesity and 44% of individuals with normal body weight), while the smallest percentage consisted of homozygous CC individuals (7% of individuals with normal body weight), and the heterozygous variant was observed in 18.7% of individuals with obesity and 49% of individuals with normal body weight. Among the TOFI and FOTI phenotypes, homozygous TT individuals accounted for 80% of individuals with obesity and 40% of individuals with normal body weight, homozygous CC individuals were observed in only 7.3% of individuals with normal body weight, and heterozygotes in 17.4% of individuals with obesity and 35.6% of individuals with normal body weight. Patients without the C allele had higher median concentrations of carbohydrate metabolism parameters and lower median concentrations of HDL cholesterol. Among patients in the control group, carbohydrate metabolism parameters were significantly higher.