Streszczenie w języku angielskim

Introduction

Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by the occurrence of cyclically repeated episodes of partial or complete upper airway obstruction accompanied by decreased arterial blood oxygenation during sleep. The consequences of OSAS include traffic accidents, increased cardiovascular morbidity, increased risk of developing metabolic disorders, behavioral and cognitive deficits. Patients with OSAS complain of decreased productivity and performance at work. It is estimated that nearly one billion people worldwide between the ages of 30-69 may have OSAS, taking the American Academy of Sleep Medicine criteria defining the syndrome when the apnea/hypopnea index (AHI) is at least 5 per hour of sleep. Due to the increasing prevalence and incidence of OSAS, it is crucial to determine which factors may be helpful in diagnosing and monitoring the course of the disease.

The pathogenesis of OSAS is multifactorial and still not fully understood. One of the hypotheses assumes the occurrence of generalized and local inflammation, caused among others by oxidative stress, which leads to repeated episodes of desaturation and reoxygenation. In patients with OSAS, chronic sympathetic nervous system activation, vascular endothelial dysfunction, and chronic inflammation underlie the development of cardiovascular disease. Major risk factors for the development of OSAS include obesity and especially central obesity directly related to the amount of the adipose tissue. These are diseases with features of chronic inflammation which creates difficulties in establishing an isolated OSAS biomarker in overweight and obese individuals. Potential biological markers include molecules associated with inflammatory response and endothelial dysfunction that may also be associated with obesity and metabolic syndrome. These include, but are not limited to, tumor necrosis factor-α (TNF-α), high-sensitivity c-reactive protein (hs-CRP), adiponectin (ADIPOQ), and leptin (LEP).

Objectives

The objectives of this study were: 1. To determine the concentration of selected adipokines (ADIPOQ and LEP) and inflammatory markers (hs-CRP and TNF-α) in serum obtained from the blood of adult patients with OSAS; 2. To assess the effect of surgery in patients with OSAS on serum concentration of selected adipokines and inflammatory markers; 3. To assess the effect of surgery in patients with OSAS on selected sleep parameters (AHI, MOS, LOS ODI), severity of daytime sleepiness, change in quality of life, and predisposition to depression and anxiety.

Material and methods

Twenty-five patients with OSAS aged 37-69 years (mean 50.2±11.3) were included in the study group. The disease was diagnosed based on type III sleep study according to the guidelines of the American Academy of Sleep Medicine, clinical history and physical examination. Eighteen patients without OSAS aged 35-69 years (mean 34.4±9.4) were included in the control group. The patients hospitalized in the Department of Otolaryngology in the University Hospital of Białystok to surgically treat otosclerosis were screened for participating in the study. Those who did not suffer from chronic diseases, immunological diseases or cancer and who accepted to participate were enrolled in the study. The study was approved by the Bioethics Committee of the Medical University of Bialystok No. 61/2016. Patients gave written informed consent for the proposed scope of study and surgical treatment. All patients in the

study group underwent surgery under general anesthesia within oropharynx (pharyngoplasty) and the base of the tongue (coblation). Patients from both groups had their blood drawn to obtain serum concentration of selected proteins: hs-CRP, TNF-α, LEP and ADIPOQ using ELISA method. Patients completed questionnaires: assessment of quality of life (36-Item Short Form Health Survey (SF-36)), assessment of excessive daytime sleepiness (Epworth Sleeping Scale (ESS)) and assessment of predisposition to depression and anxiety (Hospital Anxiety and Depression Scale (HADS)). The visual analogue scale for snoring (VAS) was used by each patient to determine the burdensomeness of snoring. All the above procedures were performed before and 9±2 months after surgery in the study group and once before stapedotomy in the control group.

Statistical analysis

In the statistical analysis, because of the limited sample size, nonparametric methods were used and medians as the primary measures of central tendency. U Mann-Whitney tests were used to compare independent samples (between the control group and the study group) for quantitative characteristics. Wilcoxon pairwise rank order tests were used to assess differences between dependent samples (assessing differences before and after treatment). Correlation relationships between pairs of quantitative variables were described using Spearman's rank correlation coefficients. All statistical hypotheses were verified at a significance level of $\alpha=0.05$. Statistical calculations were performed using IBM SPSS Statistics software version 26.0.

Results

The results of the study indicated significantly higher ($p=0.027$) serum LEP concentrations in the OSAS group (median: 7.489 ng/mL) compared to the control group (median: 3.391 ng/mL). Serum LEP concentrations decreased after surgery (median: 5.350 ng/mL). The difference was not statistically significant ($p=0.083$). There was a positive correlation of serum leptin concentrations with BMI both before ($r=0.45$; $p=0.023$) and after surgery ($r=0.44$; $p=0.027$). In our study, we obtained positive correlations of leptin with adiponectin concentrations ($r=0.56$;$p=0.003$) and with serum concentration of hs-CRP ($r=0.51$; $p=0.010$). There were significantly higher hs-CRP serum concentrations before (median: 1.782 mg/L, ($p=0.033$)) and after the surgery (median: 1.980 mg/L, ($p=0.043$)), compared to the control group (median: 0.891 mg/L). Disease severity as expressed by AHI correlated positively with serum concentration of hs-CRP ($r=0.42$; $p=0.035$), independently of obesity. We obtained significantly higher TNF-α serum concentration in the OSAS group before surgery (median: 7,999 pg/mL) compared to the control group (median: 6,000 pg/mL), ($p<0.005$). After surgery, the concentration decreased significantly (6.614 pg/mL, ($p=0.002$)).

The results of the study indicated higher adiponectin serum concentrations after the surgery in the study group (median : 14965.3 ng/mL) compared to the concentration obtained before the surgery in this group (median : 14572.5 ng/mL), which was higher in reference to the control group (median : 13651.9 ng/mL). There was no statistically significant difference in adiponectin serum concentrations between patients of the study.

Daytime sleepiness on the ESS scale in the study group before surgery (median: 13 points) was significantly reduced compared to the level after surgery (median: 5 points), ($p<0.005$).

The severity of OSAS, based on AHI, before and after surgery improved significantly from mean 34 before and 13,3 after the surgery ($p<0.005$)

Improvements were obtained in the following parameters after surgery with reference to: VAS Snoring: before surgery median: 10 points - after surgery: median: 4 points ($p<0.005$); HADS: anxiety- median decreased by 57.1%, predisposition to depression- median decreased by 66.7%. ($p<0.005$), quality of life based on SF-36 - improvement by 50% ($p<0.005$).

Conclusions

Based on the results of the study, the following conclusions were made: The concentration of selected inflammatory biomarkers (hs-CRP, TNF-α) in serum obtained from the blood of patients with OSAS may serve as an indirect indicator of the severity of inflammation. The results of this study provide support that OSAS is an inflammatory disease. Surgical treatment reduces inflammation expressed by TNF-α levels in a group of patients with OSAS. Surgical treatment for OSAS patients decreases the severity of the disease. Surgery improves the quality of life of OSAS patients and reduces their tendency to depression and anxiety.

Further studies may establish a diagnostic and therapeutic algorithm based on the determination of adiponectin, leptin, hs-CRP and TNF-α blood concentrations.