

GLUCOSE-INSULIN METABOLISM IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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ABSTRACT

There has been a great interest in the interaction between obstructive sleep apnea (OSA) and impaired glucose-insulin metabolism, but a shared intimate relationship with obesity makes discerning an independent link challenging. The aim of this study was to evaluate the prevalence of glucose abnormalities in patients suspected for OSA, referred to our Sleep laboratory. Two hundred patients with suspected OSA underwent standard polysomnography. Patients who had respiratory disturbance index (RDI) above 15 were diagnosed with OSA. In the morning after polysomnography, fasting blood levels of glucose, insulin and glycosylated hemoglobin (HbA1c) were determined, and homeostasis model assessment (HOMA) score was calculated. In the study, both OSA positive and OSA negative patients were divided according to the body mass index (BMI) in two groups: the first group with BMI ≤ 30 kg/m² and the second group with BMI > 30 kg/m². OSA positive patients with BMI ≤ 30 kg/m² had statistically significant higher blood level of insulin and HOMA index when compared to OSA negative patients with BMI ≤ 30 kg/m². There was no statistical difference in age, glucose and HbA1c level between these two groups of patients. OSA positive patients with BMI > 30 kg/m² had higher blood level of glucose, insulin and HbA1c and higher HOMA index versus OSA negative patients with BMI > 30 kg/m², but without statistically significant differences.

This study suggests that OSA could play a significant role in worsening of glucose metabolism in nonobese patients, but in obese patients, extra weight makes the impairment of glucose-insulin metabolism.

Keywords: obstructive sleep apnea, glucose, insulin

INTRODUCTION

Obstructive sleep apnea (OSA) is a common chronic disorder that is characterized by repetitive upper airway obstructions resulting in intermittent hypoxia and sleep fragmentation caused by arousals [1]. Among adults, 30–70 years of age, approximately 13% of men and 6% of women, have moderate to severe forms of OSA [2]. OSA is often closely associated with other conditions which are recognized causes of morbidity and mortality such as obesity, metabolic syndrome, insulin resistance, type 2 diabetes mellitus, atherosclerosis and systemic inflammation [3, 4]. The pathophysiological mechanisms of alterations in glucose metabolism in OSA are incompletely understood. The process is likely multifactorial and our current concept involves sympathetic nervous system overactivity, systemic and adipose inflammation, oxidative stress and hormonal alterations among the most important pathways [5]. Although the evidence for a causal link remains limited, the major characteristics of OSA, namely sleep fragmentation/deprivation and intermittent hypoxemia likely play pivotal roles as triggering factors of the pathophysiology [6]. Obesity, type 2 diabetes mellitus (T2DM), glucose intolerance and insulin resistance (IR) are common in subjects with OSA, but a shared intimate relationship with obesity makes discerning an independent link challenging [7-9]. However, the available data are somewhat controversial, since the association of OSA and insulin resistance was mostly accounted for by obesity in other studies [10-13].

The aim of this study was to evaluate the prevalence of glucose-insulin abnormalities in patients suspected for OSA referred to our sleep laboratory for polysomnography.

MATERIALS AND METHODS

The study included 200 patients. It was conducted at the University Clinic of Pulmonology and Allergy in Skopje. Inclusion criteria were age from 35 to 60 years and persistence of minimum 2 of 3 clinical symptoms of OSA. The symptoms were snoring, witnessed apnea and daytime sleepiness. Exclusion criteria were previous history and treatment of diabetes and lipid abnormalities. Body mass index (BMI) was calculated and patients were divided into two groups according to the BMI. All patients underwent polysomnography (Respironix, model Alice 5). All results from polysomnography were scored manually according to standard criteria. Apnea, hypopnea and

arousals were also identified according to the standard criteria and summarized in the form of a respiratory disturbance index (RDI). All patients with RDI above 15 were diagnosed with OSA. In the morning after polysomnography, fasting blood sample was collected from all patients. Blood levels of glucose (G), insulin (INS), glycosylated hemoglobin (HbA1c) were determined in all patients, and insulin resistance (IR) was calculated using the homeostasis model assessment (HOMA) score (fasting serum insulin (mIU/l) \ fasting plasma glucose mmol/l)/22.5) (14).

Biochemical measurements were conducted using a Hitachi auto analyzer. Serum insulin was determined with an enzyme immunoassay. Statistical analyses were performed using the Statistica software (Stat Soft). Comparisons between variables were made using the unpaired t-test for parametric data and the Mann Whitney U test (ANOVA) for non-parametric data. Statistical significance was considered at $p < 0.05$.

RESULTS

From all study patients, 51 were female with an average age of 49 ± 9 years and 149 were men with an average age of 47 ± 9 years. There was no significant difference in age, BMI and RDI between males and females. There was a significant difference in the occurrence of OSA in men versus women, 109 (73.2%) of males and 31 (62.8%) of females were OSA positive ($p < 0.03$). According to BMI, patients in the study were divided into 2 groups. There were 120 non-obese patients with $BMI \leq 30 \text{ kg/m}^2$, and 80 obese patients with $BMI > 30 \text{ kg/m}^2$. In non-obese group with $BMI \leq 30$, 62 patients were OSA negative and 58 patients were OSA positive. In obese group with $BMI > 30$, 14 patients were OSA negative, and 66 patients were OSA positive (Figure 1).

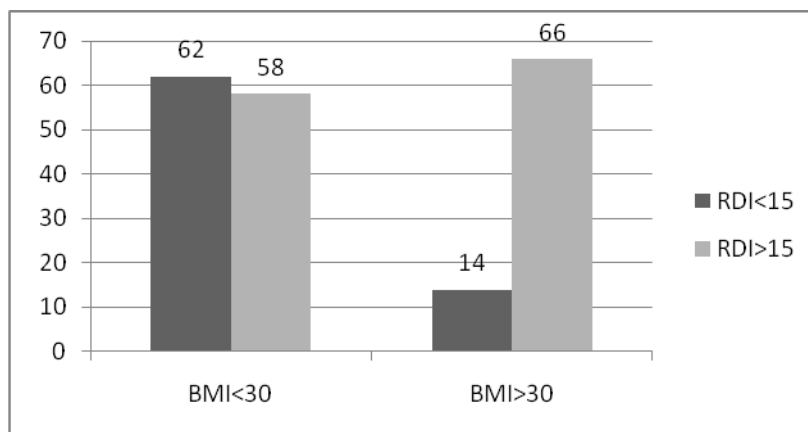


Fig. 1. Frequency of OSA in study patients divided according to BMI

In the study, both OSA positive and OSA negative patients were divided according to BMI in two groups: the first group with $BMI \leq 30 \text{ kg/m}^2$ and the second group with $BMI > 30 \text{ kg/m}^2$. OSA positive patients with $BMI \leq 30 \text{ kg/m}^2$ had statistically significant higher BMI, insulin blood level and HOMA index when compared to OSA negative patients with $BMI \leq 30 \text{ kg/m}^2$. There was no statistical difference in age, glucose and HbA1c level between these two groups of patients. (Table 1).

Table 1. Comparison between OSA positive and OSA negative patients with $BMI \leq 30$

BMI ≤ 30					
	RDI < 15 (62 pts)		RDI > 15 (58 pts)		p
	X	\pm SD	X	\pm SD	
RDI	4.65	3.41	38.68	16.92	0.000
Age (years)	47.08	9.56	47.62	8.38	NS
BMI	26.55	2.40	27.38	1.80	0.035
G (mmol/L)	5.16	0.60	5.30	0.39	NS

INS (IU/ml)	5.25	1.61	6.47	2.05	0.000
HbA1c (%)	5.17	0.32	5.20	0.25	NS
HOMA	1.21	0.42	1.53	0.54	0.000

OSA positive patients with BMI>30 kg/m² had higher blood levels of glucose, insulin and HbA1c and higher HOMA index versus OSA negative patients with BMI>30 kg/m², but without statistical significant differences (Table 2).

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Table 2. Comparison between OSA positive and negative patients with BMI>30

BM >30					
	RDI < 15 (14 pts)		RDI > 15 (66 pts)		
	X	±SD	X	±SD	p
RDI	6.81	5.01	48.26	19.17	0.000
Age	48.21	10.76	48.74	8.62	NS
BMI	32.14	1.59	34.38	3.11	0.011
G (mmol/L)	5.63	0.50	5.68	0.61	NS
INS (IU/ml)	7.29	5.07	8.17	5.04	NS
HbA1c (%)	5.44	0.41	5.48	0.37	NS
HOMA	1.82	1.20	1.98	1.33	NS

(OSA)-Obstructive sleep apnea, (RDI)-Respiratory disturbance index, (BMI)-Body mass index, (G)glucose, (INS)-insulin, (HbA1c)-glycosylated hemoglobin, (HOMA)-homeostasis model assessment.

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