Association of Obstructive Sleep Apnea Syndrome and Buerger's Disease: a Pilot Study

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Abstract- In this study we evaluated the incidence and severity of obstructive sleep apnea and Obstructive sleep apnea syndrome in patients with thromboangiitis obliterans for reduction of crisis. In 40 patients with Buerger's disease daily sleepiness and risk of Obstructive sleep apnea were evaluated using the Epworth sleeping scale (ESS) and the Stop-Bang score. An Apnea-link device was used for evaluation of chest motion, peripheral oxygenation, and nasal airflow during night-time sleep. The apnea/hypopnea index (AHI) and respiratory tdisurbance index were used for Obstructive sleep apnea syndrome diagnosis. All subjects were cigarette smokers and 80% were opium addicted. The prevalence of Obstructive sleep apnea (AHI>5) was 80%, but incidence of Obstructive sleep apnea syndrome (AHI>5 + ESS≥10) was 5% (2/40). There was no association between duration or frequency of hospitalization and Obstructive sleep apnea syndrome (P=0.74 and 0.86, respectively). In addition, no correlation between ESS and Stop-Bang scores and AHI was observed (P=0.58 and 0.41, respectively). There was an inverse correlation between smoking rate and AHI (P=0.032, r = −0.48). We did not find an association between Buerger's disease and Obstructive sleep apnea syndrome. Although the AHI was high (80%) and daily sleepiness was low. The negative correlation of smoking with AHI and on the other hand daily napping in addiction may be caused by the absence of a clear relationship between Obstructive sleep apnea syndrome and Buerger's disease.

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Keywords: Thromboangiitis obliterans; Buerger's disease; Sleep disorders; Obstructive sleep apnea syndrome

Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder, affecting approximately 5% of the middle-aged population (1,2). OSA includes a pause in respiration for more than 10 s during sleep and hypopnea includes a reduction in the number or depth of respirations, which leads to a reduction in blood oxygenation. These changes emerge as snoring and repeated awakening, accompanied by daily sleepiness, concentration problems, and memory disorders. Obstructive sleep apnea causes physiological changes such as activation of inflammatory mechanisms, a decrease in nitric oxide (NO), and an increase in catecholamine release (3-6), increased activity of the renin-angiotensin system (7,8), vascular inflammation, and spasms. These changes can cause complications such as aggravation of heart failure, ischemic heart disease, hypertension, and arrhythmia (9-13). Vascular dysfunction and endothelial inflammation as a result of obstructive sleep apnea have been also

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reported (3). Systemic inflammation plays a key role in atherogenesis, and alternate hypoxia leads to early vascular and systemic inflammatory changes (14,15). Metabolic changes caused by hypoxia lead to reduced glucose uptake, insulin resistance, and fat metabolism disorders, which increase cardiovascular risks (16,17).

Thromboangiitis obliterans is a vascular inflammation that is more common in men and is related to cigarette smoking and use of cannabis. Diagnostic criteria for Buerger's disease include cigarette smoking, onset age less than 50 years, sub-popliteal artery obstruction, the involvement of upper limbs, or thrombophlebitis in the absence of other risk factors for atherosclerosis. In one study, a relationship was found between a platelet glycoprotein allele and Buerger's disease (18).

Because of physiological and systemic changes as a result of obstructive sleep apnea, we hypothesized that sleep disorders can cause vascular spasm or could be effective in incidence or aggravation of clinical symptoms of Buerger's disease. We evaluated the incidence and severity of obstructive sleep apnea in patients with thromboangiitis obliterans.

Materials and Methods

After approval of the Deputy for Research of Mashhad University of Medical Sciences and the Regional Ethics Committee on medical thesis, this descriptive–observational study evaluated 40 patients with Buerger's disease and aggravation of clinical symptoms in the vascular surgery ward. Consent letters were obtained from all participants. Patients with anxiety disorders, depression, or convulsion as well as those who took sedative, anticonvulsant, and antipsychotic medicines were excluded.

After explaining the study methods, demographic information such as age, weight, risk factors (cigarette and cannabis), and clinical symptoms of the disease were recorded. Daily sleepiness was evaluated with the Epworth Sleeping Scale (ESS), and ESS≥10 was considered to be the pathologic state. ESS was evaluated with the rate of dozing in 8 position (24 scores). The risk of obstructive sleep apnea was also evaluated with Stop-Bang scores. The STOP-Bang questionnaire is a scoring model consisting of eight easily administered questions. In the Stop-Bang score, less than three positive responses were considered low-risk, and three or more positive responses were considered high-risk for obstructive sleep apnea. Before sleeping, an Apnea Link device (ResMed model) was connected to the patients' chest, and pulse oximetry and a nose cannula were used. Chest motions and respiratory changes, heart rate, peripheral blood oxygen percent, and nose airflow were evaluated during night sleep. The apnea/hypopnea index (AHI) and respiratory disturbance index (RDI) were used for evaluating and interpreting obstructive sleep apnea. Using the apnea/hypopnea index, 5-15, 15-30, and >30 times per hour were considered mild, moderate, and severe, respectively. Using the respiratory disturbance index (RDI), respiratory effort-related arousal (RERA) was considered along with the AHI index; this index indicated the frequency rate of apnea/hypopnea attacks and awakening during sleeping hours.

The information obtained was statistically analyzed using SPSS software (v.13). The relationship between parametric factors of patients and incidence of sleep apnea was studied using the Spearman correlation coefficient, and nonparametric factors were studied using the Mann–Whitney test. $P<0.05$ was considered statistically significant.

Results

Demographic characteristics, risk factors for thromboangiitis obliterans, sleepiness evaluation scores (ESS), and risk of obstructive sleep apnea (Stop-Bang score) before hospitalization of patients are shown in Table 1. In this study, all patients were smokers and 80% (32/40) had opium addiction.

The frequency of apnea, hypopnea, and RERA, and the AHI and RDI (RDI) are shown in Table 2 and severity of AHI and RDI are shown in Table 3. The incidence of obstructive sleep apnea when the apnea/hypopnea index was equal to or greater than 5 was 80% in patients with Buerger's disease but the incidence of obstructive sleep apnea syndrome (AHI≥5 with ESS<10) was only 5% (2 out of 40) in these patients.

No correlation was found between duration of disease and frequency of hospitalization and AHI ($P=0.74$ and $P=0.86$, respectively). There was also no association between age and AHI ($P=0.37$). In this study, no relationship was found between ESS and Stop-Bang scores and AHI ($P=0.58$ and $P=0.41$, respectively). In all patients, there were of Raynaud's phenomenon, numbness of fingers and tingling fingers, whereas symptoms of purple color change and lesion of fingers were less prevalent (90%). None of the patients complained of itching of fingers or thrombophlebitis. There was no significant statistical relationship between

clinical symptoms and evaluative scores of obstructive sleep apnea in this study. Moreover, an inverse relationship was observed between smoking rate and the AHI ($P = 0.032$ with a correlation coefficient of −0.48).

Table 1. Demographic characteristics, risk factors, Epworth Sleeping Score and Stop-Bang, score in thromboangiitis obliterans with vascular crisis

Variables		Mean (standard deviation) N (%)
Age (y)		46.8 (9.6)
Weight (Kg)		64.3 (10.5)
BMI (Kg/m2)		26.2 (8.6)
Duration of disease (y)		4.2 (1.8)
Frequency of hospitalization		2.2 (1.6)
Smoking (pack/year)		20.6 (4.6)
Addiction		32 (80%)
ESS (0-24)		1.4±1.6
StopBang	**Low risk (<3)**	24 (60%)
	High risk (≥3)	16 (40%)

Table 2. Incidence of apnea, hypopnea, respiratory effort-related arousal, apnea/hypopnea index and respiratory disturbance Index

Variables	Mean (standard deviation)
Apnea	1.9 (2.2)
Hypopnea	5.6 (3.9)
RERA	4.2 (1.5)
AHI	7.5 (5.9)
RDI	1.8 (6.4)

Table 3. Severity of apnea/hypopnea index and respiratory disturbance index

Severity of AHI (N %)	**None (<5)**	8 (20)
	Mild (5-15)	30 (75)
	Moderate (15-30)	2 (5)
	Severe (>30)	0 (0)
Severity of RDI (N %)	**None (<5)**	2(5)
	Mild (5-15)	30(75)
	Moderate (15-30)	6(15)
	Severe (>30)	2(5)

Discussion

In this study, the incidence of obstructive sleep apnea was investigated in patients with thromboangiitis obliterans to evaluate the association between sleep disorder and hypoxia with incidence of Buerger's disease, frequency of hospitalization, and clinical symptoms in patients. In the present study, 40 patients with thromboangiitis obliterans were studied. There was no significant correlation between the AHI and the respiratory disorder index, incidence of the disease, or frequency of hospitalization in these patients. Clinical symptoms such as the phenomenon of Raynaud's disease, pain, and claudication did not correlate with sleep obstructive disorder.

The most important epidemiological study on obstructive sleep apnea was the Wisconsin cohort study; in which obstructive sleep apnea (AHI≥5) was evaluated in 602 people aged 30-60 years, with the incidence found to be 9% and 24% in women and men, respectively. In this study, the incidence of obstructive sleep apnea syndrome (AHI≥5 along with daily sleepiness ES≥10) was found to be 2% in women and 4% in men (19). In a study on 1995 by Bearpark *et al.,* the incidence of obstructive sleep apnea was reported to be 3%–4% in men and 2% in women (20).

Several studies on obstructive sleep apnea and its role in various diseases such as cardiovascular disease

have done. Tascilar *et al*., 0n 2012 in 51 patients with Behcet's disease, reported the incidence of restless leg syndrome, fatigue and obstructive sleep apnea to be higher than in the control group (21). In a pilot study on 2011 by Haji-Ali *et al*., in 55 patients with Wegener's Granulomatosis, there was no correlation between sleep disorder and intensity of vasculitis or duration of the disease (22). On 2014 Burrati *et al*., in Alzheimer's patients showed that the presence of cerebrovascular disorders was correlated with the severity of obstructive sleep apnea (23). In other studies, obstructive sleep apnea has been shown to cause early atherosclerosis and increased intima-media thickness and carotid plaque formation (24,25).

In the present study, the incidence of obstructive sleep apnea (AHI≥5) was found to be 80% in patients with thromboangiitis obliterans, which was much higher than that reported in previous studies. However, only one of the patients showed evidence of sleepiness symptoms (ESS>10), and the incidence of obstructive sleep apnea syndrome was found to be 5%. This incidence was almost equivalent to levels reported for normal people in other studies. Of course, 40% of the patients had a high risk of obstructive sleep apnea as shown using the Stop-Bang risk assessment criterion.

In patients with thromboangiitis obliterans, the primary risk factor is smoking and in this study, all patients were smokers. On the other hand, the negative correlation between cigarette smoking and the AHI in this study may be one of the reasons for the absence of a clear association between obstructive sleep apnea syndrome and clinical symptoms, duration of the disease, and frequency of hospitalization of patients with Buerger's disease. Consumption of narcotics is one of the reasons for dizziness and sleepiness in addicts but is mostly denied by these patients. A high incidence of narcotics consumption (in 80% of the studied patients) may be one of the reasons for the lack of proper completion of the ESS questionnaire, which could account for the fact that using the Stop-Bang questionnaire, the risk rate was only 40% despite a high incidence of obstructive sleep apnea (AHI≥5), and only two patient (5%) had obstructive sleep apnea syndrome (AHI≥5 along with ESS>10).

Despite the high incidence of elevated AHI and obstructive sleep apnea in patients with Berger's disease, the incidence of the obstructive sleep apnea syndrome was equivalent to normal people. Considering cigarette and narcotics smoking, a case-control study on addicted patients with Buerger's disease and healthy subjects is needed to more rigorously evaluate the correlation between thromboangiitis obliterans and obstructive sleep apnea syndrome.

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