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Obstructive sleep apnea as a risk factor for cardiovascular diseases

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Abstract

Obstructive sleep apnea (OSA) is a common medical condition that occurs in approximately 5% to 15% of the population. It is usually associated with an increased risk of cardiovascular disease. Diagnosis of OSA is based on polysomnography, and its severity is measured with an apnea-hypopnea index. Most of the adverse effects of OSA on the cardiovascular system are reversible with treatment. In addition to continous positive airway pressure therapy, precautions such as weight loss, avoidance of central nervous system depressants, treatment of nasal congestion and sleeping in the lateral position may help to treat OSA. (Cardiol J 2007; 14: 534–537)

Key words: obstructive sleep apnea, cardiovascular system

Introduction

Obstructive sleep apnea (OSA) is a disorder, characterised by repeated episodes of breath cessation during sleep, which is usually seen together with daytime sleepiness and/or altered cardiac function. It is usually associated with increased cardiovascular morbidity and mortality [1].

The main objectives of this paper is to summarize the pathophysiological and clinical aspects of OSA and to discuss its cardiovascular effects and the treatment of this condition.

Definition and frequency

Sleep apnea is defined as a cessation of breathing activity during sleep due to either dysfunction of the central respiratory control mechanisms or a mechanical collapse and obstruction of the upper airways. The former is known as central sleep apnea and the latter as OSA [2].

Obstructive sleep apnea is the more common form of sleep apnea and occurs in approximately 5% to 15% of the population [2, 3]. It is characterized by hypopnea and apnea intervals leading to a 4% decrease in oxygen saturation usually in overweight patients who suffer from daytime sleepiness [2]. During collapse periods the pharynx is partially or

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completely closed and sleep is fragmented, so patients suffer from daytime sleepiness [4]. The apnea-hypopnea index (AHI), which is the number of apneic and hypopneic events per hour, is used to determine the severity of sleep apnea, defining apnea as mild if AHI is between 5 and 15, moderate between 15 and 30 and severe if AHI is above 30. Cardiovascular risk is increased in patients whose AHI is over 30 per hour [5].

The effects of obstructive sleep apnea on the cardiovascular system

Although known to be a benign disease, retrospective studies have shown that OSA is usually associated with increased morbidity and mortality due to systemic and/or pulmonary hypertension, heart failure, myocardial infarction and stroke [1]. However, it is good to remember that most of the adverse effects of OSA on the cardiovascular system are reversible with treatment. Moreover, continuous positive airway pressure (CPAP) ventilation therapy has been shown to have cardioprotective effects and to decrease mortality and morbidity among those patients. Increased cardiovascular risk in OSA is independent of confounding factors such as obesity, hyperlipidemia or metabolic disease [6].

The effects of OSA on the cardiovascular system can be divided into long- and short-term implications. Short-term effects are known to be related to mechanical effects such as sudden intrathoracic pressure changes, hypoxia, hypercapnia induced chemical substance release, sympathetic-mediated vasoconstriction, increased after-load, increased left ventricular transmural pressure and arousal from sleep. However, long-term effects are the results of some complex dysfunctions which are not very well known. Autonomic dysfunction (mainly by repetitive increase in sympathetic tone), malfunctioning of the carotid body, production of free oxygen radicals, decreased nitric oxide levels and endothelial dysfunction, pro-inflammatory changes (increased levels of cell adhesion molecules, interleukin 6, tumour necrosis factor alpha and C-reactive protein), tendency to coagulation by increased thrombocyte aggregation, higher leptin levels and enhanced atherosclerosis are potential mechanisms for long term effects [4, 6, 7].

It has been shown that manoeuvres such as induction of hypoxia can cause blood pressure changes during sleep [8]. Systemic arterial hypertension, with a prevalence of 50%, is the leading cardiovascular abnormality that is related to OSA [9]. The association between OSA and hypertension is independent of age, sex, previous blood pressure history, body mass index and smoking [10, 11]. Hypoxia and hypercapnia induced sympathetic activation, increased endothelin and decreased nitric oxide levels and hence endothelial dysfunction, increased arterial stiffness and vascular resistance are possible mechanisms behind this predisposition [12]. In a prospective follow up of 709 patients, Peppard et al. [10] found that OSA was predictive of the presence of hypertension four years later.

Associated with OSA, pulmonary hypertension is seen approximately 30%, coronary artery disease 20–30%, congestive heart failure 10%, and stroke can be seen as much as 10%. Arrhythmias are the other disorders which can be induced by OSA during the sleep period [13].

Obstructive sleep apnea is an independent risk factor for coronary artery disease. Increased C-reactive protein and oxidative stress, hypoxia itself, increased sympathetic activity, tachycardia, cardiac oxygen demand increase, increased systemic vascular resistance, increased tendency to thrombosis and many other unknown mechanisms cause an increased risk for coronary events in OSA patients. Moreover, in a study by Tan et al. [14] interestingly it was found that OSA has a negative effect on the preventive functions of high-density lipoprotein, which contributes to the effect of OSA increasing the risk for coronary artery disease.

Obstructive sleep apnea associated heart failure has a prevalence of approximately 10% [11, 15]. Besides causing left ventricular systolic function impairment through the well-known causes of heart failure such as hypertension and coronary artery disease, OSA can directly affect the ventricular functions [11, 16, 17]. Increased sympathetic drive, increased endothelin and endothelial dysfunction, increased systemic vascular resistance, inflammatory cytokines and transmural pressures are well-known OSA induced mechanisms deteriorating ventricular systolic and diastolic functions [4]. Tanriverdi et al. [16] illustrated that OSA patients exhibited a mild decrease in left ventricle systolic function, which was not attributable to the well-known causes of left ventricle dysfunction. They concluded that aortic elasticity was also deteriorated and increased aortic stiffness might be responsible for many of the cardiovascular alterations caused by this disease. Likewise, a cross sectional cohort study by Phillips et al. [18] concluded that systemic arterial stiffness was positively correlated with the severity of OSA.

Obstructive sleep apnea is also associated with an increased risk of stroke, independent of any

other cardiovascular risk factors [19]. The factors that may increase the risk of stroke in OSA include acute reduction in cerebral blood flow due to apnea, hypoxemia and prothrombotic state and a tendency towards atherosclerosis, and hypertension. Stroke is an important cause of mortality and morbidity among patients suffering from OSA [4, 11, 19, 20].

Obstructive sleep apnea is associated with a broad range of arrhythmias such as atrial fibrillation (AF), sinoatrial or atrioventricular block, sinus node dysfunction, bradyarrhythmia and asystole. Rhythm disturbances such as bradycardia are known as a typical feature of OSA [21]. Additionally, a study by Harbison et al. [22] showed the presence of a relationship between rhythm disturbances and the severity of OSA.

Hypoxia and apnea induced vagal tone increase trigger, especially nocturnal bradyarrhythmias. Therefore, physicians have to evaluate carefully any nocturnal dysrhythmia in terms of OSA coexistence in order not to make an unnecessary pacemaker implantation decision [4, 11]. Consequently, in such a case, only CPAP therapy may successfully overcome the arrhythmia [19]. The hypoxemia, sympathetic overactivation, pressure surges, increased cardiac wall stress and transmural pressures may increase the likelihood of AF in OSA patients. Furthermore, in patients who underwent cardioversion for AF, if sleep apnea is accompanying, there is a twofold increase in the risk of recurrence of AF within 12 months compared with OSA patients treated with CPAP. Accordingly, CPAP therapy in OSA patients is shown to decrease AF recurrence [4, 23].

Reynolds et al. [24] showed that among OSA patients, heart rate variability increased as apnea severity increased. However, during REM sleep there was a decrease in heart rate variability which also suggested autonomic dysfunction in OSA patients. Yang et al. [25] found that there were changes in heart rate turbulence of the OSA patients in the absence of overt cardiac disease, which correlates with the severity of OSA and are again related to the abnormalities in cardiac autonomic activity.

Besides systemic hypertension, long lasting OSA can cause pulmonary hypertension and right ventricular failure without any underlying pulmonary or cardiovascular disease [11].

Diagnosis and treatment

Patients possibly having OSA were identified using the Epworth Sleepiness Scale (an eight-item questionnaire assessing sleep quality and symptoms related to OSA). The standard test for OSA diagnosis is polysomnography including electrocardiography, oxygen saturation measurements, electroencephalography, electro-oculography, snoring microphone and assessment of body positions by video recording with an infrared camera for the whole night during the patient's habitual sleep hours. Polysomnography shows an obvious drop in tidal volume — a decrease in oxygen saturation during the apnea and hypopnea episodes which are terminated by an arousal detected by EEG [26].

Precautions such as weight loss, avoidance of central nervous system depressants, treatment of nasal congestion and sleeping in the lateral position may help to treat OSA, as well as CPAP, the noninvasive treatment shown to normalize oxygen saturation, improve regulation of systemic and pulmonary hypertension, improve cognitive performance and mood, decrease somnolence and improve daytime alertness and quality of life and reduce mortality [27–30]. CPAP treatment may also prevent nocturnal ST-segment depression, improve left ventricular systolic and diastolic functions, improve functional class and decrease the risk of cardiac arrhythmias in patients with heart failure [31]. In recent years, a number of automatic CPAP systems in the variable-pressure mode have been in use, which has resulted in decreased overnight cumulative CPAP levels, which seems to improve the efficacy and tolerability of OSA treatment [32]. Other than noninvasive treatment strategies, surgical procedures to overcome the obstruction such as uvulopalatopharyngoplasty, laser uvulopalatoplasty, tonsillectomy, partial resection or ablation of the tongue, reconstruction of the mandible or maxille and tracheostomy may be used for selected cases [24, 32].

Conclusions

Obstructive sleep apnea is a common, treatable but underdiagnosed disease state, which should be kept in mind by physicians dealing with cardiovascular disorders. Sleep quality has to be a part of routine history taking in cardiovascular practice because a broad spectrum of cardiovascular disorders can be effectively prevented merely by treating OSA. Because of its systemic effects, many other disease states such as pulmonary thromboembolism or even aortic aneurysm and dissection are areas for concern that should be studied for a direct association with OSA [26, 33].

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