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Sleep apnea and comorbid diseases - a review

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Abstract

Obstructive sleep apnea (OSA) is a common disease spreading around the world. It is unavoidably linked to the increasing rate of obesity, particularly in Western societies. Associated higher prevalence of sleep disordered breathing has also been observed. There are many diseases that can lead to OSA and many that are a result of untreated OSA. From the widely known cardiovascular complications to indirectly related diseases, such as insomnia, Alzheimer's disease or psoriasis. Overall, sleep-disordered breathing have been shown to negatively impact quality of life, including general health perception, physical functioning, social functioning, and vitality. That is why it is important to spread awareness about OSA, often asymptomatic, through medical staff and patients in the risk group. In this review we describe the illness, the ways to diagnose it and discuss comorbid diseases.

Key words

sleep apnea, sleep-disordered breathing, cardiovascular complications, positive airway pressure

Introduction

Approximately 39 million U.S. adults have obstructive sleep apnea (OSA). 936 million adults around the world are estimated to have mild to severe OSA [1]. The exact numbers are

hidden, because it is a challenge to diagnose the disease as long as patients remain asymptomatic. In an already diagnosed group of patients we have easy to apply treatment. Sleep apnoea has been linked to significant daytime functioning deterioration and cardiovascular morbidities, and as a result it is causing significant increase in mortality [2]. Nonetheless, there are a lot of diseases that can induce OSA. That is why it is crucial to raise awareness among the populations with risk factors and among medical staff.

Definition: sleep - disordered breathing

Sleep-disordered breathing (SDB) refers to a range of sleep-related breathing disorders: primary snoring, OSA, central sleep apnea (CSA), Cheyne-Stokes respiration, and sleep-related hypoventilation. [3] Obstructive sleep apnoea is known for recurrent upper airway collapse, intermittent hypoxia and fragmented sleep [4], which affect the patient with fatigue, dangerous daytime sleepiness and possible cardiovascular diseases. Upper airways obstruction leads to two consequences: arousals from sleep and oxyhemoglobin desaturations. Apneas and hypopneas occur in all phases of sleep, but are more common in N1, N2 and rapid eye movement (REM) sleep stages than in N3 sleep [5]. In this paper we focus on obstructive sleep apnea because of its high incidence rate.

Diagnosis

The most common symptoms of OSA have been already counted - normally the patient notices them by himself or the person sleeping with the patient in one room observes snoring or pauses in breathing. Other symptoms are unrefreshing sleep, morning headache, nocturia, choking sensation during sleep and cognitive function decline. [6] In cases with obvious symptoms and comorbid diseases we can use a pulse oximeter in diagnosis at a patient's home. In more unclear cases short hospitalization is needed to perform polysomnography. Polysomnography (PSG) is an overnight test conducted when a patient is asleep in a sleep lab with a sleep technologist in attendance. The following report contains information about the patient's sleep, limb movements, and the presence of sleep disordered breathing. [7]

Diseases co-occurring with sleep apnea

Obesity and overweight are the most common risk factors of OSA. Obesity is a disease itself, but there is no one way to come down with it. In fact, we are more and more aware of diseases that can result in obesity and further in OSA. For example, psoriasis is known to increase the risk of obesity. The prevalence of OSA among patients with psoriasis varies

across studies from 36% to 81.8% compared with 3–7% in the general population and it increases with the duration of psoriasis and is higher in cases of severe psoriasis and psoriatic arthritis. [8] Another condition, insomnia, one of the epidemics of our century, increases insulin resistance which can result in weight gain [9]. It makes a snowball effect and after some time it can co-occur with OSA. On the other hand, there is a possibility in which OSA leads to insomnia. Apnoeas are associated with cortical arousals from sleep. Short interruptions of sleep may be perceived as awakenings or continued wakefulness if they are brisk and repeated. [10] In addition, nocturia, one of the symptoms of OSA, may deteriorate insomnia. Finally, apnoea-induced arousals that are associated with sensations of breathlessness may increase anxiety and further worsen co-existing mental illnesses, such as depression or anxiety disorders.

OSA is often associated with cognitive impairment. Also, there is a link between OSA and Alzheimer's disease biomarkers of neurodegeneration, in the young and middle-aged group of patients. OSA patients have longer reaction times in tasks requiring sustained or selective attention or vigilance, and show an increase in reaction times in conditions requiring divided attention. [11]

Cardiovascular diseases

Another disease, diabetes, is strongly related to OSA. A systematic review of 41 studies of adults with diabetes showed 60% OSA prevalence. [9] Diabetes or insulin resistance is a part of a metabolic syndrome associated with obesity, hypertension, hyperlipidemia and atherosclerosis. The syndrome often co-occur with OSA. However OSA as a single disease can provoke hypertension and other cardiovascular complications such as arrhythmia, myocardial infarction, coronary artery disease and heart failure. During non-rapid-eye-movement sleep (approximately 80% of total sleep time), sympathetic activity decreases and parasympathetic activity increases. OSA disrupts sleep and the process of lowering blood pressure and heart rate. [12] Severe OSA is associated with higher odds of incident hypertension, stroke and cardiovascular death due to increased nocturnal sympathetic activation and cyclic hypoxemia, oxidative stress and prolonged inflammation. [13] In a group of patients admitted to the hospital for heart failure decompensation, OSA has been highly prevalent, which means it is a cause of coronary disease and heart damage, verified in many studies. [14] In non-alcoholic fatty liver disease (NAFLD), a few epidemiological studies have suggested that OSA may be an important risk factor, independent of obesity. The

insulin resistance and the hypoxic burden of sleep apnea are investigated in this pathophysiology. [15]

Other influences

Sleep apnea severity has been linked to several types of cancer development and malignancy, especially pancreatic and kidney tumors. [16] Sleep disturbance aggravates pain perception, meaning fragmented sleep may lead to chronic pain. The effect is stronger in women and has not been yet explained. [17] In fact, even pregnancy or childbirth complications could be triggered by OSA [18]. High estrogen levels can lead to a nasal congestion and by that to the upper airways narrowing. Women with objectively diagnosed OSA have the risk for preeclampsia more than double, whereas risks for gestational hypertension nearly double. The risk for cesarean section also increased significantly among women with either subjective or objective sleep disordered breathing. The severity of gestational OSA generally improves after delivery, but women diagnosed with or suspected of having OSA during pregnancy should be followed postpartum to determine whether OSA has resolved or requires further treatment. [18]

Nasal disorders

The nasal airway plays a significant role in breathing during sleep. Not only are obesity-related conditions responsible for OSA, but craniofacial anatomy malformations are crucial too, along with nasal obstruction. It is a common comorbidity in OSA. 70% of patients with OSA had nasal obstruction confirmed by clinical examination and rhinomanometry. [19] Changes to the nasal mucosa, such as rhinitis or polyps may contribute to nasal obstruction. The most frequently used medications are topical nasal steroid sprays, which have been shown to improve sleep quality, but not necessarily sleep apnea. Nasal surgery alone has a small effect in reducing the OSA, however it can improve the quality of life in a daytime by effortless breathing.

Craniofacial malformations causing OSA should be considerate individually, treated, if possible, by maxillo-facial surgery. Patients with neuromuscular diseases require a multidisciplinary team in this case. [20]

Treatment

Positive airway pressure therapy is the gold standard for treatment of patients with moderate to severe OSA, though poor adherence to this therapy is a significant problem. Devices

deliver a pressurized column of air to open the airway in patients with sleep apnea. [21] That can be uncomfortable and irritating during sleep and takes the patient's cooperation. Changing lifestyle and weight reduction are helpful, however it takes time and patient's commitment. Also, there is no certainty of overweight relapse. [22] Other ways of treatment, such as surgery and pharmacology, were tested, but with not sufficient efficacy. Only sulthiame has promising outcomes, but requires further studies. [23]

Quality of life

Finally, it is necessary to mention how the quality of life of patients suffering because of OSA changes. Fatigue and daytime sleepiness may deteriorate depression and overall well being. In addition, severe sleepiness of vehicle drivers can lead to traffic crashes, injuries or even death. Tired patients are often irritated, which influences the relations in family and at work. OSA compounds their health, physical condition and career. Diagnosis and treatment of sleep disorders is critical for patients afflicted by these conditions. [11, 14, 24]

Summary

In this review we focused on diseases directly and indirectly linked to sleep apnea, to highlight the importance of diagnosis for this condition, both for medical staff and patients. It is not commonly known how many symptoms OSA provokes or that a proper treatment can be a critical point for patients' well being and quality of life. We recommend taking care of a patient in a comprehensive way, remembering co-occurrence of cardiovascular diseases with other disorders. Treatment of OSA is easy to introduce and highly efficient, simulating normal breathing during the sleep and by that restraining symptoms and possible complications.

Author's contribution

Conceptualization: Urszula Guderska; writing - rough preparation: Urszula Guderska, Agnieszka Urbanek, Jacek Kurzeja; writing - review and editing: Urszula Guderska, Agnieszka Urbanek, Jacek Kurzeja, Danuta Maciejewska, Adrianna Rasmus-Czternasta, Magdalena Bartczak, Filip Czternasty.

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