Obstructive Sleep Apnea: Brief Introduction

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Nearly a billion adults around the world are affected by a disease that is characterized by upper airway collapse while sleeping called obstructive sleep apnea or OSA. The progression and lasting effects of untreated OSA include an increased risk of diabetes mellitus, hypertension, stroke, and heart failure. There is often a decrease in quality-of-life scores and an increased rate of mortality in these patients.

obstructive sleep apnea (OSA)

1. Pathophysiology

1.1. Sympathetic Nervous System

Sleep is typically characterized by the dominance of parasympathetic activity in the body. Decreased oxygen and increased CO_2 caused by an airway obstruction lead to increased sympathetic output in the periphery and central chemoreceptors [1][2]. Increased sympathetic output remains present during sleep and while awake. The study conducted by Narkiewicz et al. compared sympathetic responses among obese patients with or without OSA. The study showed that an increased sympathetic response was found in obese patients with OSA but was not found in the control obese group without OSA [2]. Because the obese patients without OSA did not have an increased sympathetic response, it is possible that OSA is the causative factor for having an increased sympathetic response [3]. The renin-angiotensin-aldosterone system (RAAS) is activated by the sympathetic neurons and, since the sympathetic response is found to be upregulated in patients with OSA, the RAAS system is also overstimulated. Patients with OSA often have elevated angiotensin II and aldosterone hormone levels in the body. Increases in these levels lead to water retention in the kidneys and vasoconstriction in the peripheral vasculature [4]. As a result of these mechanisms being activated, hypertension is commonly found in patients with OSA [5].

1.2. Endothelial Dysfunction

Endothelial cells normally release vasoactive and vasorelaxant factors to regulate the vascular tone. In OSA, the endothelial cells do not function in the same capacity [6]. Phillips et al., in a prospective study of OSA patients, measured oxygen saturation, hemodynamics, and changes in circulating endothelin-1 levels [7]. The study found that, after OSA treatment, patients experienced decreases in blood pressure and endothelin-1 [7][8]. Nitric oxide, which normally serves as a vasodilator, was found to have impaired action in OSA; however, the impaired action was reversible after CPAP treatment [9].

1.3. Systemic Inflammation

In OSA, there are increased inflammatory biomarkers such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-a) [10][11][12]. This condition can be considered a low-grade chronic inflammatory disease [10][11][12]. In addition to the inflammatory biomarkers, concentrations of reactive oxygen species are increased due to the hypoxia caused by the night-time intermittent airway obstruction [13]. Increased reactive oxygen species in addition to the inflammation biomarkers mentioned above indicate a possible mechanism by which OSA increases risk of cardiovascular disease and overall mortality.

1.4. Metabolic Dysfunction

Type 2 diabetes mellitus (T2DM) is more prevalent in OSA populations. This is notable because T2DM may increase all-cause mortality and the risk of CVD. In a cross-sectional analysis of 2588 participants, the Sleep Heart Health Study found a link between obstructive sleep apnea and elevated fasting glucose, decreased glucose tolerance, and diabetes mellitus [14]. Nadeem at al. conducted a meta-regression analysis determining that there was increased LDL, triglycerides, and total cholesterol in patients with OSA [15]. This is notable because increases in these factors as well as blood glucose are risk factors for cardiovascular disease.

2. Risk Factors

Risk factors that can cause OSA include obesity, gender, age, and genetic syndromes [16]. Screening patients for these risk factors and understanding the etiology of OSA is essential for beginning treatment to prevent economic burden and health risks.

2.1. Obesity

Obesity is a hallmark risk factor for the manifestation and disease progression of OSA [17]. Adipose is deposited around the circumference of the neck and airway of obese patients and may lead to increased risk of pharyngeal collapse. Airway collapse causes mechanical obstruction from fat buildup and is accompanied by loss of neural control that contributes to the development of OSA [18]. A study by Peppard et al. showed that there is a direct relationship between weight gain and OSA prevalence and apnea-hypopnea index (AHI), which is calculated as the number of episodes of obstructive apnea divided by the number of hours of sleep. A 10% increase in body weight increased the prevalence of moderate–severe OSA and AHI by six times [16][19]. Researchers at the Harvard T.H. Chaan School of Public Health speculate that one in two (48.9%) adults in the United States will become obese and that 25% will have severe obesity by the year 2030 [20]. It is predicted that the prevalence of OSA will increase as the prevalence of obesity increases in the years to come [21].

2.2. Gender

Men seem to be affected by OSA more than women. The SHIP-Trend study showed than men were at a greater baseline risk of obstructive sleep apnea than women by analyzing the prevalence of OSA in 1280 participants, with the result that OSA prevalence was 59% in the men studied compared to only 33% in the females [22]. Another study performed by Whittle et al. showed via MRI that men often have more fat deposition in the neck compared to

women [23]. Men′s increased fat disposition causes increased neck circumferences and consequently puts them at a higher risk of airway collapse compared to women. Additionally, men′s airways tend to be longer than those of women. It is hypothesized that the extended airways put men at a higher risk of pharyngeal collapse [24]. Comparing individuals with the same BMI, OSA tends to be less prevalent in women compared to men [25]. The prevalence difference observed with gender is thought to be due to the role of sex hormones during the fertile age, which tend to disappear after menopause, and may influence the prevalence and severity of OSA in older females [26].

2.3. Age

Older-aged individuals are at a higher risk of having OSA. The previously mentioned SHIP-Trend study found that aging steadily increased the prevalence of AHI in men and women beginning at the age of 50 [22]. The suspected mechanism of how age influences OSA prevalence is from decreased genioglossus reflex to negative pressure, which impairs dilator muscle′s ability to compensate from pharyngeal collapse. Increases in type 1 collagen lead to delayed contractile-relaxant response in the pharyngeal constrictor muscle [27][28]. Because this compensatory response is decreased and the level of type 1 collagen in the pharyngeal constrictor muscle is increased, the contraction and relaxation response that is supposed to occur with each inspiration and expiration while sleeping is delayed [27][28]. The United Nations′ 2019 report on World Population Ageing completed by the Department of Economic and Social Affairs estimates that the proportion of the population over the age of 65 will increase from roughly 9% in 2019 to about 16.7% by the year 2050. This increase in elderly population, in tandem with the expected increase in obesity, is expected to result in an increased prevalence of OSA [29].

3. Signs and Symptoms

The patient may be largely unaware that they are exhibiting signs or symptoms of obstructive sleep apnea since they occur while the patient is asleep. Ascertaining a history from a spouse or partner of the patient is vital to completing a workup of their condition. The patient may be aware that they snore, or perhaps that they wake up gasping for air; however, their partner will likely be more aware of the frequency and severity of these signs. Frequent complaints from the spouses or patients with OSA include drowsiness, headaches upon waking, xerostomia, sore throat, and unrestful sleep. Daytime sleepiness or fatigue despite sufficient opportunities to sleep that is unexplained by other medical problems are other symptoms that can occur in OSA. Patients with OSA frequently present with a recessed mandible, a high Mallampati score, a high BMI, and a limited pharyngeal space [30][31][16]. Screening for obstructive sleep apnea consists of using either the yes or no questions in the STOP-BANG questionnaire or the Berlin questionnaire [30][1][16]. STOP-BANG questions include yes or no questions about the patient′s symptoms of drowsiness, absence of breathing during sleep, presence of hypertension, BMI more than 35 kg/m^2, older than 50 years of age, neck circumference greater than forty centimeters, and male gender. If the screening produces a result indicating the presence of OSA, there is a recommendation for a sleep study utilizing polysomnography either at the patient′s home or in a lab [16].

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