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Review Article

A Review on Complications of Sleep Apnea

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Abstract

Sleep apnea occurs when the upper airway repeatedly becomes blocked during sleep, reducing or entirely blocking airflow. This is referred to as obstructive sleep apnea. If the brain fails to provide the necessary impulses for breathing, the disease is known as central sleep apnea. Sleep apnea and other sleep breathing problems are a leading cause of medical, social, and occupational disability. Sleep apnea is also linked to pulmonary hypertension, cardiac arrhythmia and other neurocognitive effects, majority of individuals with sleep apnea go undetected, putting them at danger during surgery. It is critical to identify these patients so that relevant steps can be implemented as soon as possible. In this review article, we will discuss about sleep apnea issues and their possible causes.

Keywords: Sleep apnea, Bradycardia, Tachycardia, Breathing, Hypercapnia

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Introduction

Sleep-disordered breathing refers to brief, frequently cyclical, cessations in breathing rhythm (apneas) or brief or continuous reductions in breath amplitude (hypopneas) that are severe enough to produce arterial hypoxemia and hypercapnia. These apneas and hypopneas are sleep-related and are accompanied by [1] a compromised, often completely closed, extrathoracic upper airway ("obstructive" event); [2] a significant reduction or cessation of brain stem respiratory motor output ("central" event); and a combination of central and obstructive events. These ventilatory deficiencies, together with the resulting occasional hypoxemia, frequently produce transitory arousals from sleep and sleep state fragmentation throughout the night and autonomic nervous system overcompensation. [3, 4] The most common clinical symptoms are Loud snoring, choking/gasping, apneas observed by the bed partner, extreme tiredness and weariness, and a morning headache. The patient's and their family's quality of life is severely impacted by sleep apnea. Sleep apnea can have consequential health problems if it is not properly treated; it raises the risk of hypertension, type 2 diabetes, and cardiovascular disease. [5] Sleep apnea is also a well-known cause of cognitive impairment. [6]

Sleep Apnea

Sleep apnea is a main sleep disorder marked by interruptions in breathing while sleeping. Obstructive sleep apnea (OSA), central sleep apnea (CSA), and complex sleep apnea are the three basic kinds of sleep apnea. Obstructive apnea is defined as a pause in airflow lasting at least 10 seconds caused by the collapse of the upper airway during sleep. In contrast, during a central apnea, airflow is interrupted when there is a lack of attempt to breathe, which usually originates from the brain respiratory centers to the muscles that govern breathing. Some people have a combination of obstructive and central apnea, which is known as complex sleep apnea [7]

An Apnea-Hypopnea Index between 5 and 14 is considered mild sleep apnea, between 15 and 29 is termed moderate sleep apnea, and more than 30 episodes per hour is considered severe sleep apnea. Several sleep apnea screening measures have been created to detect at-risk patients. [8]

Complications of Sleep Apnea

Cardiac Arrythmia

Obstructive sleep apnea syndrome is usually associated with potentially life-threatening arrhythmias. [9-14] Bradyarrhythmias can be caused by vagal activity, and sympathetic overactivity can promote a variety of rhythm abnormalities, including ventricular arrhythmias. The most prevalent cardiac rhythm abnormality identified in OSA patients is significant sinus arrhythmia (also known as cyclic variation of heart rate), which is characterized by bradycardia during the apneic phase followed by tachycardia on restart of respiration. This arrhythmia is almost universal in patients with severe OSA and has been considered as a predictor of a positive OSA diagnosis. [15]

Bradycardia results from parasympatetic hyperactivity, whereas tachycardia results from waking from sleep and vagal withdrawal in the postapneic period. Although the actual processes behind the association between OSA and cardiac arrhythmias are unknown, it is possible that they are similar to those hypothesized for other cardiovascular illnesses. OSA is marked by a pharyngeal collapse that occurs repeatedly during sleep, pursued by oxyhemoglobin desaturation, prolonged inspiratory efforts against an obstructed airway, and sleep awakening. [16] These mechanisms elicit several of the autonomic, hemodynamic, humoral, and neuroendocrine responses that cause acute and chronic alterations in cardiovascular function on their own. These side effects could lead to cardiac arrhythmias or other types of cardiovascular illness connected to OSA. [17-19] Nonsustained ventricular tachycardia, sinus arrest, second degree atrioventricular conduction block, and frequent (>2 bpm) premature ventricular contractions are the most prevalent arrhythmias during sleep. [20-24] The link between OSA and arrhythmias was discovered over 30 years ago. Tilkian et al. used continuous overnight Holter electrocardiographic, respiratory, and electroencephalographic recordings to inspect the effect of atropine and tracheostomy on cardiac arrhythmias during awake and sleep in 15 patients with sleep-induced obstructive apnea. [25]

Sleep was linked with marked sinus arrhythmia (93%), extreme sinus bradycardia (40%), asystole (33%), second degree atrioventricular (A-V) block (13%), ventricular arrhythmias—complex premature ventricular beats (66%), and ventricular tachycardia (13%). Premature ventricular beats were the only arrhythmias that occurred when awake (40%). The findings revealed that OSA is characterized by significant sinus arrhythmia during sleep, which is commonly accompanied by potentially life-threatening tachyarrhythmia and bradyarrhythmia. [26]

Hypertension

The strong link among OSA and hypertension is remarkable. According to studies, 30–40% of hypertensive patients test positive for OSA, and 50% of those diagnosed with OSA have a history of hypertension. [27, 28–30] These findings show that OSA and hypertension are both common, and that they usually coexist, OSA is characterized by repeated bouts of oxyhemoglobin desaturation and reoxygenation. This could explain why blood pressure is rising, because chemoreflex-mediated increases in sympathetic activity cause peripheral vasoconstriction. [27, 31, 16] Another mechanism activated by OSA that adds to development of high blood pressure is the renin–angiotensin–aldosterone system, which is also caused by intermittent hypoxia. [32]

This is supported by the existence of greater levels of aldosterone and angiotensin II in OSA patients, as well as the decrease in these hormones following CPAP treatment. [33] Furthermore, increased oxidative stress and decreased production of endothelium-dependent vasodilator molecules like nitric oxide aggravate vascular dysfunction and systemic inflammation. [34, 35] OSA has long been known to escalate the risk of hypertension, especially in the elderly. [36-38] The OSA-related blood pressure profile is typically characterized by decreased or absence of nocturnal sleep dipping, owing to escalated sympathetic activity at night. [27, 39] Excessive sympathetic activity, in combination with other vasoactive substances released in response to hypoxia, most certainly leads to daytime hypertension. In addition to these mechanisms, OSA may be related with more frequent or severe hypertension due to increased aldosterone release, at least in individuals with resistant hypertension, where a substantial association between serum aldosterone concentration and severity of OSA has been reported. [40,-42]

OSA is characterised by the repeated closure of the upper airway during sleep. Five or more apneas per hour of sleep are considered abnormal, and seriously affected patients have hundreds of apneas each night, resulting in recurrent hypoxemia and hypercapnia. Apneas are followed by increases in sympathetic activity to peripheral blood vessels, resulting in vasoconstriction. [43] The majority of apneas and hypopneas are terminated by a brief waking from sleep followed by brief hyperventilation. Both arousals and blood gas changes cause acute sympathetic activation and higher catecholamine levels [44,45], as well as a rise in heart rate and arterial pressure, which is particularly noticeable during post-apneic hyperventilation and can reach values as high as 240/130 mmHg.

Sleep and sexual disfunction

Sleep apnea has an impact on both male and female sexual functions. Erectile dysfunction, in particular, has been a frequently observed sexual dysfunction in men with OSAS. Continuous positive airway pressure (CPAP) treatment has been demonstrated to help these patients. [46, 47]

Female sexual function is linked to complicated neurophysiological and psychosocial processes. The pathogenesis of sexual dysfunction in women with OSAS is complex. Endothelial dysfunction has been shown to play an important role. [48-50] The pudendal nerve is the primary innervator of the vaginal tract. The pudendal nerve's integrity is critical for normal female sexual function. It has been shown that peripheral neuropathy can develop in OSAS, and that the severity of the chronic intermittent nocturnal hypoxia is connected to it. [51]

Testosterone levels have been shown to be lower in women with OSAS, and this has been linked to disease severity. [52] Women's sexual dysfunction may also be influenced by their quality of life and mood. [(46)] Males with OSAS, sexual dysfunction has been extensively described. Sexual dysfunction has been observed to affect 30 to 50 percent of males with OSAS. [53, 54] There have been a relatively small number of research on sexual dysfunction in females with OSAS. Koseoglu et al. [55] discovered a significant frequency of decreased sexual function in a prospective study of pre-menopausal women with OSAS in Turkey. They also discovered that, with the exception of satisfaction and discomfort, all scores in sexual function categories declined considerably as the severity of OSAS increased.Erectile dysfunction (ED) is a common complaint in middle-aged and elderly men. Intermittent nocturnal hypoxia is likely to add to reduced penile tumescence by increasing endothelial dysfunction and altered vasoregulation, which may be

mediated by decreased nitric oxide (NO) generation as well as elevated levels of endothelin levels. [56–58]

Several studies have found a significant rate of ED in male OSA patients, ranging from 47.1 % to 80.0 %. [60-64] The severity of OSA is thought to be a significant determinant in the development of ED [65, 66], but this conclusion is inconsistent. [67] Shin et al found that ED is associated with lower minimum oxygen saturation rather than AHI. The underlying mechanism of interaction between OSA and ED is unknown, while numerous possibilities have been presented, including a hormonal influence of testosterone, hypoxemia-induced peripheral neuropathy, or vascular endothelial dysfunction. [68]

Male OSA patients have lower blood testosterone levels, according to many researches, and there is a negative relationship between AHI, oxygen desaturation index, and testosterone level. [61, 65, 69] Testosterone, on the other hand, is suspected to play a role in the etiology of sleep apnea, and testosterone supplementation may exacerbate the problem. Giving testosterone to hypogonadal patients raised the number of apneas and hypopneas significantly, according to Schneider et al. [70] In a similar study, Cistulli et al [71] found that testosterone injection exacerbated the OSA of a 13-year-old Marfan's syndrome child. As a result, the relationship between testosterone and OSA is complex, and treating an OSA patient with testosterone should be done with caution. The relationship between ED and peripheral nerve dysfunction is supported by an altered bulbocavernous reflex in OSA patients, a routinely used method for diagnosing pudental neuropathies. [53] Furthermore, the increased levels of inflammatory markers such high-sensitivity C-reactive protein, tumor necrosis factor a, interleukin (IL)-6, and IL-8 in patients with severe OSA and ED suggests that vascular endothelial dysfunction is involved in the pathophysiology of ED in OSA. [72]

Respiration

The respiratory system is a primary cause of sleep disturbances, including some of the most serious and frequent sleep disorders. The circadian timing system has a big influence on sleep–wake state regulation, [73] and fresh evidence suggests it can also influence respiratory control. [74, 75] As a result, it's been proposed that the circadian timing system may be involved in the occurrence or severity of numerous sleep-related respiratory disorders. Walsh and co-workers" roentgenographically established the relevance of upper airway blockage in inducing sleep fragmentation and arousal by exhibiting retraction of the tongue creating apposition with the posterior pharyngeal wall during the apneic phase. The persistence of paradoxical thoracoabdominal motions with accompanying rhythmic swings in intrapleural pressure indicates continued rhythmic activity of the respiratory center during the stoppage of airflow. During obstructive apnea, pleural and supraglottic pharyngeal pressures showed similar breathing variations, demonstrating patency of the glottis and lower airway and showing that the occlusion lay above this level, according to Remmers et al. Just before the onset of obstructive apnea, there may be a rapid drop in tone in the upper airway muscles. These factors, together with the diaphragm's continuing contraction, cause subatmospheric pressures in the pharynx, producing tongue retraction and further narrowing of the airway. Fiberoptic endoscopy demonstrates invagination of the posterolateral pharyngeal walls during the apneic periods. [76] The apneic episode continues until arousal occurs, possibly as a result of hypoxic stimulation of the reticular system of the CNS. The resulting increase in motor neuron activity preferentially activates the upper airway musculature, [77] resulting in termination of the obstruction and resumption of ventilation. Periods of alternating obstructive apneas and arousals may occur throughout the entire night and as many as 400 to 500 episodes may be present.

Sleep has a substantial impact on breathing and gas exchange in the respiratory system, which may aggravate the dysfunction seen while awake in respiratory disorders such as COPD and asthma. [78] Additionally, sleep-related respiratory illnesses such as obstructive sleep apnea (OSA) can co-exist with other chronic respiratory diseases and worsen sleep-related breathing abnormalities [79] Sleep quality is reduced in patients with chronic respiratory disease, [80] and decreased sleep efficiency with a reduction in REM sleep has been reported in patients with COPD, which correlates with awake arterial oxygen tension (PaO2) but not with the degree of airflow obstruction, [81] despite the fact that lung hyperinflation has been linked to poor sleep quality in COPD patients. [82]

Changes in respiratory control, respiratory muscle function, and lung mechanics are all symptoms of sleep deprivation. Reduced brain inputs to the respiratory centre, decreased respiratory motor neuron output, decreased chemoreceptor sensitivity modifying ventilatory responses to hypoxia and hypercapnia, and increased upper airway resistance are all respiratory control effects. [83, 84] Respiratory muscle activity, particularly accessory muscles of breathing, is compromised during rapid eye movement (REM) sleep, however diaphragmatic contraction is unaffected. [85] Skeletal muscles, including the accessory muscles of respiration, are actively inhibited in normal REM sleep, although diaphragm contraction is generally retained [86]. Changes in functional residual capacity and perturbations in ventilation–perfusion connections have also been documented as negative effects on lung mechanics. [87] Overall, these physiological effects cause hypoventilation, hypoxemia, and hypercapnia, which can be detected in normal persons to a modest and clinically unimportant degree. [88] Physiological alterations during sleep, especially during REM sleep, may be enough to cause clinically substantial disruptions in gas exchange in patients with chronic respiratory diseases such COPD. [89] In COPD, where lung hyperinflation reduces the efficacy of diaphragmatic contraction, patients become more reliant on accessory muscle contraction to sustain breathing, the loss of accessory muscle activity in REM sleep is especially essential. [90]

In addition, disrupted ventilation–perfusion interactions lead to hypoxemia, which increases the degree of nocturnal oxygen desaturation caused by physiological hypoventilation during sleep. [87, 89] Airflow blockage is worsened by sleep and the supine position, [91] which can increase hyperinflation and hypoventilation in COPD patients. Hyperinflation increases the amount of work required to breathe, resulting in increased arousability and sleep disruption. In addition, lower skeletal muscle contraction, particularly during REM sleep, leads to upper airway obstruction by reducing the ability to endure upper airway collapsing forces during inspiration. [92]

Narcolepsy

Narcolepsy is a chronic sleep condition marked by severe daytime sleepiness and, in the vast majority of cases, cataplexy. Patients with narcolepsy may also experience sleep paralysis, hypnagogic hallucinations, or hypnopompic hallucinations (hallucinations that occur as the person falls asleep. [93, 94] Narcolepsy is a very uncommon condition. However, due to the inadequacy of current diagnostic criteria, the exact frequency and prevalence remain

unknown. Narcolepsy and narcoleptic borderland conditions (particularly NT2) may be more common than previously thought [95] Narcolepsy should be addressed as a worldwide hypothalamic condition rather than just a sleep disorder in the clinic. Patients with narcolepsy experience a variety of motor, cognitive, psychological, emotional, metabolic, and autonomic problems in addition to tiredness and sleep disorders. Despite the fact that these problems are currently poorly described and understood, they are most likely the result of underlying hypothalamic malfunction in orexin signaling and related neural networks. Narcolepsy is caused by well-known genetic variations, as well as still poorly understood environmental exposures and probably epigenetic factors. Between idiopathic, familial, and secondary types of the disease, the magnitude (and character) of these aetiological contributions is likely to differ. Systematic evaluations, such as neuroimaging investigations and measures of inflammatory markers (such as cytokines and CD8+ and CD4+ lymphocytes) as well as narcolepsy comorbidities, may give light on potential disease-causing or disease-modifying factors. Emerging data from human and rodent illness models suggests that immunological pathways are involved in the death or silencing of orexin neurons. [96, 97, 98] If this information is valid, it will have far-reaching implications, as it will allow for the early detection of incomplete phenotypes, the selection of suitable treatment (symptomatic versus immunomodulatory), and possibly even the prevention of narcolepsy in predisposed individuals. Orexin insufficiency is a key component of the pathophysiology of narcolepsy, albeit the specific processes are yet unknown.[99]

Conclusion

Sleep is essential for all living things. Sleep deprivation has been linked to a wide range of problems in most physiological systems, including endocrine, metabolic, higher cortical function, and neurological illnesses. Sleep disorders can emerge as complaints of insufficient sleep, an excess of perceived sleep, or abnormal movements during sleep. Sleep disorders should be treated as soon as possible since they can have a major detrimental impact on quality of life and daytime function.

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