REVIEW ARTICLE

Sleep-disordered breathing and stroke

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Abstract

Sleep disordered breathing is an emerging disorder with effect on several health conditions. The association of sleep disordered breathing with cerebrovascular disorders has been relatively recent but shows it as a highly prevalent albeit neglected accompaniment in all kinds of stroke. Moreover, its presence has been found to be not just associated with incidence of strokes but also with overall poorer outcomes in stroke survivors. The spectrum of disorders with its special impact on both ischemic and hemorrhagic strokes is reviewed.

Introduction

Breathing disorders include two main subdivisions of clinical conditions like the central sleep apnoea and periodic breathing and the continuum of upper airway resistance syndrome and Obstructive sleep apnoea (OSA). Whereas the central sleep apnoea and its associated periodic breathing patterns have their origins as well as are implicated in a large variety of neurological conditions, it is the latter condition comprising the continuum from the upper airway resistance syndrome (UARS) through snoring and OSA that is chiefly implicated in stroke. It is for this reason that the latter two are together called sleep disordered breathing (SDB).

Sleep apnea is the most common of the sleep disordered breathing occurring in 5-15% of the population[1]. On the other hand it has been seen to have a prevalence greater than 50% in patients with ischemic stroke[2]. The importance of the association is aggravated by the commonness and variety of the manifestation. Snoring, the most common and vital accompaniment of OSA has been reported in prevalence to vary from 5-87% in men and 2-57% in women[3]. However, to say that all snoring, irrespective of the cause is implicated in strokes would be an over simplification. It is important to rule out the various nonapnoeic causes of snoring which cause many side effects but not to the extent that UARS and OSA have on cerebrovascular disease[4]. In fact, it is the number of sleep disturbances occurring in UARS and OSA that has been mainly implicated to cause dysfunction in cerebrovascular hemodynamics.

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Some terminology used in the assessment of Sleep apnea

Apnea in adults is defined as the absence of airflow at the nose or mouth for 10 s or more. Hypopnea is defined as a 30% or more reduction in airflow from baseline that lasts 10 s or more, with or without significant desaturation (more than 4% from baseline)[5]. Patients with SDB and stroke may also present with Cheyne-Stokes breathing (CSB) which is characterized by cyclic fluctuations in breathing drive, hyperpneaalternating with apneas or hypopneas in a gradual waxing and waning fashion.

SDB as a cause of stroke

Some of the earliest studies of stroke conducted investigating the association between snoring and stroke showed relative risks varying from 1.26 to 10.3[6,7]. However, the exposure assessments in these studies were

personal interviewing or mailed questionnaire about habitual snoring, and lacked objectivity. The definitive studies giving a quantified estimation of SDB and stroke were polysomnography based.

Several case control and cohort studies using polysomnography in patients with stroke showed prevalence rates varying from 60 to 80 percent[8]. The studies showed that the strength of this association was similar to traditional risk factors for stroke such as hypertension, smoking, atrial fibrillation, and hypercholesterolemia and held true even after controlling for confounders.

Apart from its direct effect on cerebrovascular effects, sleep apnoea has been known as a cause of systemic hypertension causing a rise of mean arterial pressure to the extent of 40mmHg even after controlling for confounding factors like age, sex, BMI, alcohol, and smoking[9]. The normal 15-20% drop in blood pressure during night time as compared to daytime is also absent in patients with sleep apnea[10]. Its effects on being directly associated with other leading causes of mortality including myocardial infarction, congestive heart failure and atrial fibrillation are also seen as a provocative factor for stroke and cerebrovascular disorders.

Sleep Apnea as a consequence of stroke

Sleep apnea was established as a consequence of stroke in one of the earlier studies comparing patients recovering from hemispheric stroke versus controls matched for age, body-mass index and, risk factor profile[11]. Several case reports have shown the association of SDB with bulbar stroke[12]. Neurological dysphagia has also been shown to occur after hemispheric stroke which along with facial weakness which can lead to secondary sleep disordered breathing in these patients and worsen neurological recovery[13].

Is the occurrence of sleep disordered breathing similar in different types of stroke?

A prospective study investigating the prevalence and behavior of sleep disordered breathing showed no relationshipbetween SDB events and the topographical parenchymatous location of the neurological lesion or vascular territory. Similarly rates of SDB were found to be comparable between the different stroke subtypes[14].

Manifestations of sleep apnea in stroke patients

Breath pattern during sleep in these subjects is marked by partial or complete block of the upper airway manifested through snoring with intermittent apneas and arousals. The sleep pattern is grossly distorted with maintenance insomnia and excessive daytime sleepiness along with episodes of daytime naps, snoring, and even apnoea episodes[1]. Most patients with sleep apnea share similar clinical profile with features of metabolic syndrome, such as central obesity, insulin resistance, and systemic hypertension[15].

Functional outcome of stroke associated with SDB

Whether the sleep related respiratory events occur before or as a consequence of the cerebrovascular event, the functional consequences are shared and range from an overall unfavourable clinical recovery to early neurological worsening, delirium, depression and other mood disorders, reduced cognition, and a longer period of hospitalization and rehabilitation[16]. Several epidemiological studies done in middle aged adults have shown sleep apnoea to have association with diminished attention and concentration, and in severe cases with impaired executive function and manual dexterity. These results could accrue from the repeated exposures to hypoxia to regional perturbations in cerebral vasculature. White matter disease was also associated significantly more in the apnoea group as compared to normal population[17]. Whereas, daytime vigilance and majority of the neuropsychological deficits improved with therapy, impaired manual dexterity and, planning deficits persisted despite therapy[8].

Pathophysiology of sleep disordered breathing

The pathophysiology of sleep disordered breathing involves multiple mechanisms that interact with each other to lead to an ischemic event. There occurs systemic hypertension occurring secondary to a chronically elevated heart rate with altered hemodynamics and endothelial dysfunction. Patients with SDB can experience repetitive episodes of hypoxia or reoxygenation during transient cessation of breathing that may promote systemic oxidative stress and inflammation.

Long term SDB also means presence of rhythm disturbances and oxidative stress which leads to cerebrovascular accidents[18–21]. [Fig-1]

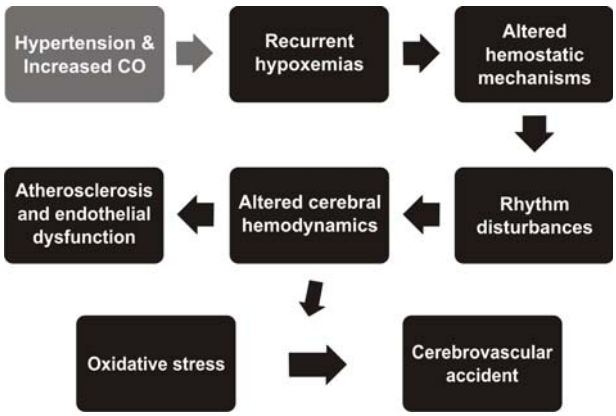

Figure 1: Mechanism of damage caused by sleep disordered breathing.

Diagnosis of sleep disordered breathing after stroke

In-laboratory PSG is the standard investigation for the diagnosis and management of OSA. A full-night PSG can be aimed to simultaneously record multiple physiologic variables, including a limited EEG, electrooculogram(EOG), chin and leg EMG, airflow via thermal and pressure changes, oximetry, abdominal and thoracic movement, snoring, and ECG. Data from EEG, EOG, and EMG leads can be used to evaluate sleep architecture and efficiency as well as identification of arousals and limb movements. A variety of portable devices are also available to record the full montage of signals recorded in a routine PSG. The SATS trial studying the feasibility of a randomized sham-controlled CPAP also switched to portable monitoring early in the study due to logistical difficulties and intolerance issues arising from a comprehensive in-laboratory PSG during the acute stroke period[18].

Management strategies for sleep apnea in stroke

Various modalities have been tried towards treatment of sleep apnoea for improvement of various parameters from weight loss and posture training to nasal and other assist devices for opening and securing airways during sleep. CPAP remains the cornerstone in the management of sleep apnoea. The earliest retrospective cohort study for treatment of sleep apnea studying tracheostomy versus conservative treatment of weight loss dated back to the 1970s favoring tracheostomy over the latter in improving vascular outcomes[7].

Later in 2005, an observational study comparing the incidence of fatal and nonfatal cardiovascular events in simple snorers, patients with untreated OSA, those treated with CPAP, and healthy controls showed that patients with untreated severe disease had a higher risk of fatal and non-fatal cardiovascular events compared to those with mild to moderate snorers and simple snorers. Multivariate studies for risk of fatal and non-fatal cardiovascular events in patients with severe obstructive sleep apnoea–hypopnoea showed odds ratio=2.87, 95% CI 1.17–7.51 and 3.17, 95% CI 1.12–7.51, respectively[19].

Continuous positive airway pressure in stroke

The use of CPAP has faced continuous debate regarding its utility in improving stroke outcomes in patients with stroke. In some of the earlier studies, the application of CPAP as the mainstay of management for patients with sleep apnea was found not just to improve symptoms and quality of life but also lower risk of nocturnal hypertension and overall mortality[20]. Due to the overwhelming positive result with administration of CPAP in sleep apnoea patients it was not possible to design a randomized control trial for CPAP versus conservative management in patients with sleep apnoea. Some studies discussing the feasibility of CPAP in patients with acute ischemic stroke showed significantly reduced apnea-hypopnea score in patients using CPAP (32.2±25 versus 3-9.8±6.6, $p<0.001$) with no significant increase in nursing burden ($p=0.741$) and significantly greater NIHSS improvement in patients using CPAP compared to controls[21].

However, a study by the Parra et al.[22] shows the effect of nasal CPAP in patients of ischemic stroke ($n=71$) followed up for 2 years showed accelerated neurological recovery and delayed appearance of cardiovascular events but showed no improvement in survival or quality of life. A similar although smaller study in 22 patients showed improved functional and motor, but not neurocognitive outcomes in patients of stroke undergoing rehabilitation.

Other treatment modalities for sleep disordered breathing and stroke

A retrospective cohort study carried out in Taiwan on 10,339 subjects tried to compare the incidence of cerebrovascular disease in those receiving uvulopalatopharyngoplasty (UPPP) versus those who did not. It showed a statistically higher rate of incidence of cerebrovascular disease in patients who did not receive UPPP versus those who underwent surgery (5.14% versus 1.06%, respectively)[23].

Conclusion

The occurrence of sleep disordered breathing has grave prognostic significance in patients of ischemic stroke. Its presence can be an inciting factor as well as a consequence of the clinical event and the treatment of the condition, regardless of the etiology can have significant improvement in the functional outcomes after stroke as well as reduce the recurrence of a subsequent ischemic event.

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