SHORT COMMUNICATION

Mechanisms that Link Obstructive Sleep Apnea to Stroke

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Abstract

Obstructive sleep apnea (OSA) is a chronic sleep-related breathing disorder characterized by recurrent episodes of partial or complete collapse of the upper airway during sleep, despite an ongoing effort to breathe. OSA has been demonstrated to be an independent risk factor for ischemic stroke, atrial fibrillation, arterial hypertension, coronary artery disease, and myocardial infarction. The mechanisms that link OSA to stroke include cardiac arrhythmias, autonomic dysfunction, hypertension, hypoxia, inflammation, and dyslipidemia. Treatment of OSA can lead to primary prevention of stroke and can secondarily reduce other vascular risk factors causing stroke.

Keywords: Obstructive sleep apnea, Stroke.

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Introduction

Obstructive sleep apnea (OSA) is a chronic sleep-related breathing disorder characterized by recurrent episodes of partial or complete collapse of the upper airway during sleep, despite an ongoing effort to breathe.[1] The symptoms of OSA include snoring, excessive daytime sleepiness, fatigue, morning headaches, irritability, nonrefreshing sleep, and memory loss.[2] It is an underdiagnosed condition and it is believed that around 85% individuals with clinically significant sleep apnea have never been diagnosed.[3]

Stroke is the fifth leading cause of death in the US and the leading cause of long-term adult disability. Stroke can be broadly divided into hemorrhagic and ischemic strokes. Hypertension is an important risk factor for hemorrhagic stroke and also contributes to atherosclerotic disease. Atherosclerosis can lead to ischemic stroke. Hyperlipidemia is also an important risk factor for stroke as it leads to atherosclerosis of intracranial and extracranial blood vessels. Atrial fibrillation is a well-recognized risk factor for cardioembolic stroke.[4]

Obstructive sleep apnea has been demonstrated to be an independent risk factor for ischemic stroke, atrial fibrillation, arterial hypertension, coronary artery disease, and myocardial infarction.[5] The mechanisms that link OSA to stroke include cardiac arrhythmias, autonomic dysfunction, hypertension, hypoxia, inflammation, and dyslipidemia. Treatment of OSA can lead to primary prevention of stroke and can secondarily reduce other vascular risk factors causing stroke.[6]

This article is an attempt to highlight the association of OSA with autonomic dysfunction, hypertension, increased inflammatory response, and atrial fibrillation. It will also look upon the evidence that suggests OSA to be an independent risk factor for stroke.

OSA and Autonomic Dysfunction

An autonomic response is triggered in response to stress signals such as hypoxia and apnea. It is crucial in maintaining blood flow and oxygen supply to vital organs. During hypoxia, chemoreceptors are activated which cause hyperventilation to increase oxygen delivery to the blood. The activated sympathetic system leads to vasoconstriction and redistribution of blood to vital organs. Parasympathetic activation leads to bradycardia which reduces the myocardial oxygen demand. This is an oxygen-conserving reflex and is similar to the diving reflex seen in seals and ducks. It also occurs in humans during facial immersion in water and apnea.[7] Hypoxia also causes pulmonary vasoconstriction which can lead to right heart failure. Frequent and sustained episodes of apnea contribute to the high blood pressure at night.[6]

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OSA and Hypertension

It has been found that individuals with sleep apnea have a higher mean 24 hours blood pressure and night-time blood pressure and it increases with the severity of the sleep apnea.[8] This nondipping blood pressure during the night is a risk factor for cardiovascular disease.[6] A strong association has been found between untreated OSA and treatment resistant hypertension.[9] Continuous positive airway pressure (CPAP) therapy for OSA has been shown to reduce hypertension.[6]

OSA and Inflammation

The apneic episodes in OSA initiate the inflammatory cascade and cause the inflammatory markers such as IL-1, IL-6, TNF-α, and interferon γ to rise in the blood. These inflammatory markers damage the endothelial lining of the blood vessels. They also cause aggregation of platelets which leads to further vascular endothelial damage and oxidative stress. This repeated damage can lead to cardiovascular disease and stroke. The sympathetic stimulation also releases catecholamines which lead to increased blood pressure and further vascular damage.[5] CPAP therapy administration for a period of 6 months has been proved to decrease the level of inflammatory markers in the blood.[10]

In a study conducted on ischemic stroke patients, increased TNF-α levels were found in patients who had OSA as compared to those without it, suggesting it to be an important inflammatory marker linking stroke and OSA.[11] TNF-α levels were also found to be increased in pediatric OSA patients. These levels dropped following surgical treatment of OSA in these patients.[12]

OSA and Atrial Fibrillation

The prevalence of atrial fibrillation in patients with sleep apnea has been found to be between 3 and 5% as compared to 1% in the general population.[6] When compared to patients without sleep apnea, patients with untreated OSA were found to have a higher risk of recurrence of atrial fibrillation after successful cardioversion. Treatment with CPAP is associated with a significant reduction in the recurrence of arrhythmia and this is independent of age, BMI, diabetes, or hypertension.[13]

The arrhythmia can be a result of the autonomic system activation and hemodynamic responses triggered by the apnea.[13] The vagal output in the heart is increased during the apneic episodes of OSA due to the negative intrathoracic pressure.[13] This enhances the inducibility of atrial fibrillation.[13] The combination of these neurohumoral, hemodynamic, and metabolic stresses along with the increase in circulating catecholamines and inflammatory mediators increase the risk of atrial fibrillation in OSA patients.[6,13]

OSA and Stroke

The Sleep Heart Study showed that OSA increased the risk of ischemic stroke. It found men with moderately severe OSA to have almost a threefold increased risk in ischemic stroke as compared to men with no or mild apnea.[14] This risk of stroke increased 6% with every unit increase in baseline obstructive apnea-hypopnea index from 5 to 25.[14] The result was consistent even after adjustment of the possible confounding factors.[14] A significant association was also found between snoring and cerebral infarction.[15]

Individuals with OSA were found to have worse outcome after stroke as compared to individuals without OSA. Individuals who had a definitive diagnosis of OSA before suffering an acute ischemic stroke had an increased risk of death within the first month after the stroke.[16]

Conclusion

Obstructive sleep apnea increases the risk of stroke as an independent risk factor and due to its association with hypertension, increased inflammatory response, autonomic dysfunction, and atrial fibrillation. It is also associated with a poor prognosis after stroke. Treating OSA can decrease the risk of stroke and prevent its recurrence.

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