

Effect of one night nasal continuous positive airway pressure treatment on the endothelial function in patients with obstructive sleep apnea

Obstrüktif uyku apnesi olan hastalarda endotel fonksiyonu üzerine bir gece sürekli nazal pozitif hava yolu basıncı tedavisi etkisi

Obstructive sleep apnea (OSA) is the most prevalent cause of sleep-related breathing disorders and moderate to severe OSA affects between 7- 14% of men and 2-7% of women in the general population (1). OSA is characterized by excessive, recurring episodes of complete or partial upper airway blockage during sleep that cause transient oxygen desaturation, hypercarbia, and central nervous system arousal. Untreated OSA may cause acute cardiopulmonary failure: acute respiratory failure, acute congestive heart failure, and sudden death (2) and is also associated with a panoply of chronic systemic disorders (3). These conditions include hypertension, coronary artery disease, cardiac dysrhythmias, congestive heart failure, cerebrovascular accident, renal dysfunction, diabetes, and depression (3). The pathophysiologic mechanisms relating OSA and its protean consequences are incompletely defined but are believed to involve intermittent hypoxemia and hypercarbia, sleep fragmentation, and intrathoracic pressure changes that may lead to ischemia-reperfusion causing oxidative stress and generating reactive oxygen species that cause NO-mediated endothelial dysregulation and the activation and promulgation of inflammatory pathways (4). The cardiopulmonary alterations that occur during an obstructive event cause autonomic nervous system dysregulation that persists into wakefulness and may contribute to the systemic consequences of OSA (5).

The most common form of treatment for OSA is continuous positive airway pressure (CPAP) which is usually delivered by a nasal or oro-nasal mask. The positive airway pressure acts as a pneumatic stent to prevent upper airway occlusion and maintain airway patency. CPAP effectively reduces the number of apneas and hypopneas and improves oxygenation during sleep. OSA-related hypertension, cardiac dysrhythmias, depression, and stroke are reduced by effective CPAP treatment (6-9).

CPAP treatment is also associated with improvements in the endothelial dysfunction observed in untreated OSA. Oyama et al. (10) showed that forearm blood flow response to reactive hyperemia improved after three months of CPAP thera-

py in individuals with OSA and the metabolic syndrome. They also measured increases in plasma nitric oxide levels and decreases in asymmetrical dimethylarginine, thiobarbituric acid reactive substance, soluble Fas ligand, soluble CD40 ligand, tumor necrosis factor-alpha, interleukin (IL)-6 and IL-8. Using another measure of endothelial function, strain gauge venous occlusion plethysmography after intra-arterial infusion of sodium nitroprusside (an endothelium-independent vasodilator) or acetylcholine (an endothelium-dependent vasodilator), Buechner et al. (11) demonstrated impaired endothelial function in individuals with untreated OSA that improved after treatment with CPAP. Other studies have shown a progressive increase in flow-mediated vasodilation of the brachial artery one and two weeks after CPAP treatment for OSA that was associated with increased plasma concentrations of nitric oxide species and decreased asymmetric NG, NG-dimethylarginine concentration (12). CPAP reduces measures of oxidative stress and increases nitric oxide species (13). CPAP withdrawal from patients with OSA who had been adequately treated with CPAP causes a progressive increase in endothelial dysfunction measured by flow mediated dilation that begins within one week of CPAP withdrawal and continues for at least another week (14).

In this issue of The Anatolian Journal of Cardiology, Tulmaç et al. (15) utilized brachial artery flow dilation to measure endothelial function in patients with newly diagnosed OSA before and after a CPAP titration study. These patients had severe OSA with a mean apnea-hypopnea index (AHI) of 60.6. CPAP treatment was very effective, and reduced the mean AHI to 9.6 and ameliorated significant oxygen desaturation events. Flow mediated dilation increased from 8.55% before CPAP to 12.08% after CPAP suggesting an acute improvement in endothelial function after only one night of CPAP treatment. In contrast, serum C-reactive protein values did not change after the CPAP titration. The authors conclude that the acute improvement in flow mediated dilation after the initiation of effective CPAP treatment suggests that acute pathophysiologic factors such as increases in

Address for Correspondence/Yazışma Adresi: Ralph J. Panos, MD, Pulmonary, Critical Care and Sleep Division, Cincinnati Veterans Affairs Medical Center Cincinnati, OH 45220- USA Phone: 513/861-3100 ext. 4500 Fax: 513/487-6670 E-mail: ralph.panos@va.gov

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vasodilating factors or reductions in vasoconstricting substances may mediate the improvement in endothelial dysfunction.

These results, although preliminary and from a small cohort of patients with severe OSA, are intriguing and suggest that CPAP may have significant salutary effects on vascular function in individuals with OSA and these benefits occur within one night of CPAP use. The mechanisms mediating the observed improved vascular dilation after CPAP treatment remain to be established.

Another potentially important clinical consequence of Tulmaç et al. (15) observations is that the beneficial effect of CPAP may be ephemeral (at least if the beneficial effect declines as rapidly as it starts). Thus, endothelial dysfunction may resume after as short a period as one night of CPAP non-adherence. The clinical implication might be that nightly adherence with CPAP is essential for maximal and sustained benefit. Further studies of the kinetics of the application and withdrawal of CPAP on vascular function are required.

Like many innovative studies, Tulmaç et al. (15) observations generate further questions about the kinetics and mechanisms through which mechanical stenting of the upper airway by externally applied positive airway pressure is transduced into biological signals culminating in the clinical benefits of CPAP treatment for OSA.

Ralph J. Panos

**Pulmonary, Critical Care, and Sleep Medicine Division,
Cincinnati Veterans Affairs Medical Center and University
of Cincinnati School of Medicine, Cincinnati-USA**

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