Editorial Comment

Impaired Autonomic Function in Patients with Obstructive Sleep Apnea

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There is growing evidence that obstructive sleep apnea syndrome (OSAS) may contribute to the initiation and progression of hypertension and heart failure. OSAS may have direct and deleterious effects on cardiovascular function and structure through several mechanisms, including sympathetic activation, oxidative stress, inflammation, and endothelial dysfunction.

Continuous positive airway pressure (CPAP) treatment prevents airway collapse during inspiratory efforts. Treatment with CPAP results in acute and marked reduction in nocturnal sympathetic nerve traffic (*1*) and blunts blood pressure surges during sleep (*2*). Effective long term treatment of OSAS by CPAP has been shown to improve blood pressure control (*3*–*5*), neurohumoral factors and cytokines (*6*).

In an article appearing in this issue of *Hypertension Research* (*7*), Noda *et al*. studied the effect of long term CPAP therapy on baroreflex dysfunction and endothelial dysfunction in patients with moderate to severe OSAS. Impairment of baroreflex function may be a potential mechanism linking OSAS to an increased risk of hypertension. Furthermore, decreased heart rate variability and increased blood pressure variability might increase the risk of future hypertension and hypertensive end-organ damage.

They evaluated changes of R-R intervals during phase IV of the Valsalva maneuver as a baroreflex function. It may be impossible to quantify the intensity of stimulation by this method. However, this method is very attractive because it is simple and safe, can be performed without sophisticated equipment, and yields reproducible results. The baroreflex sensitivity (BRS) index for phase IV of the Valsalva maneuver, and the Valsalva ratio were both significantly lower in patients with OSAS compared to controls in their study. Previous studies have reported that increased sympathetic drive during wakefulness and repetitive surges in blood pressure during sleep might reduce BRS or reset the baroreflex function curve to higher levels of pressure (*8*, *9*). These studies may indicate that OSAS is related to autonomic dysfunction.

Successful CPAP therapy improved the BRS index and Valsalva ratio in the present study by Noda *et al*. (*7*). Therefore, successful CPAP therapy may attenuate sympathetic hyperactivity and hyperresponsiveness to hypoxia. Narkiewicz *et al*. (*10*) reported that muscle sympathetic nerve activity (MSNA) decreased after 6 months and 1 year of CPAP therapy. Thus CPAP therapy is the most effective therapy for reducing high sympathetic activity in patients with OSAS.

The authors also pointed out an interesting mechanism related to the regulation of sympathetic outflow. Nitric oxide (NO) is implicated in the regulation of sympathetic outflow in the central nervous system (*11*). The increase in plasma NO_x concentration after one night of CPAP therapy may contribute to the attenuation of sympathetic hyperactivity. Impairment of endothelial function and inhibition of NO production in OSAS may be implicated in the OSAS-related hypertension.

The diagnosis of OSAS is clinically important. Indeed, the most recent JNC guidelines place sleep apnea at the top of the list of causes of secondary hypertension (*12*). OSAS should be strongly suspected in obese individuals with resistant hypertension, those with the absence of a nocturnal decrease in blood pressure, and those with symptoms suggestive of OSAS (snoring, and excessive daytime somnolence). Additionally, the recognition of OSAS as a disease related to auto-

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nomic dysfunction helps us understand why circulatory and respiratory regulations are impaired in patients with OSAS-related hypertension and heart failure. Sleep apnea therapy by CPAP will be an additional effective treatment for these patients.

To achieve better neural circulatory control, further studies will be required to find more precise and simpler clinical methods to evaluate the severity of autonomic dysfunction in patients with OSAS.

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