Sleep is more than a break from life

Bernd M. Sanner and Martin Tepel

1 Department of Medicine, Bethesda Krankenhaus, Hainstr. 35, 42109 Wuppertal, Germany; and 2 Medizinische Klinik IV, Charite Campus Benjamin Franklin, Berlin, Germany

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This editorial refers to ‘Pulmonary hypertension in obstructive sleep apnoea: effects of continuous positive airway pressure. A randomized, controlled cross-over study’ by M.A. Arias et al., on page 1106

Man spends one-third of his life in sleep. Sleep is not a passive state but rather an active process that if disturbed on a regular basis can even constitute a threat to man’s health. Sleep medicine is a fairly new discipline and until 1980 there were only few scientific publications on the theme. Obstructive sleep apnoea syndrome was first described in 1976 by Guilleminault. Since then it has turned out to be a disorder that does not only cause a noise problem for the patient’s bed partner but also constitutes a serious disease of overriding importance.

Obstructive sleep apnoea syndrome is highly prevalent: 17–24% of adults have sleep-related breathing disorders and 2–4% of them suffer from the disease and need treatment. In addition, obstructive sleep apnoea is associated with an increased risk of cardiovascular disease and stroke, and there is a strong suspicion that untreated sleep-disordered breathing precipitates greater mortality. Gami et al. reviewed polysomnograms and the death certificates of 112 Minnesota residents who had undergone polysomnography and had died suddenly from cardiac causes. They found that people with obstructive sleep apnoea have a peak in sudden death from cardiac causes during the sleeping hours, which contrasts strikingly with the nadir of sudden death from cardiac causes during this period in people without obstructive sleep apnoea and in the general population.

Obstructive sleep apnoea is characterized by intrathoracic pressure swings during obstructed breathing, hypoxaemia as a result of apnoeic events, and arousals from sleep that terminate the apnoea. The resultant hypoxaemia can lead to nocturnal cardiac ischaemia and ventricular arrhythmias. Apnoeic episodes elicit increased sympathetic activity, acute blood pressure elevations, and platelet aggregation. These factors can all be responsible for the increased mortality and the increased risk of stroke in sleep apnoea patients.

Although the causal association between obstructive sleep apnoea and night-time hypertension has always been well accepted, the relation to daytime hypertension was less clear until recently. This is because of the fact that patients with hypertension and patients with obstructive sleep apnoea have common risk factors like obesity (and its pattern of distribution), alcohol consumption, age, male gender, and decreased physical activity. Several well-conducted, large population-based studies have now been able to prove an independent association with a dose-response relationship between these two conditions in man, indicating that obstructive sleep apnoea constitutes a risk factor for hypertension. These results induced the National High Blood Pressure Education Program of the National Heart, Lung, and Blood Institute to publish updated consensus recommendations for the prevention and treatment of hypertension and to declare obstructive sleep apnoea as an identifiable cause of hypertension in their JNC 7 report. Given the high prevalence of obstructive sleep apnoea, this disease could be the most frequent (treatable) cause of hypertension.

Several investigators have reported an association between obstructive sleep apnoea and sustained daytime pulmonary hypertension. Approximately 20% of patients with obstructive sleep apnoea—as determined by right heart catheterization—have pulmonary hypertension. Sustained pulmonary hypertension among these patients is often related to right ventricular failure. In this context, the report of Arias et al. extends the existing knowledge.

Pulmonary hypertension in patients with obstructive sleep apnoea is often associated with obesity or chronic obstructive lung disease. However, Arias et al. examined patients without coexisting cardio-pulmonary disease and they could demonstrate that the level of pulmonary hypertension is directly related to the severity of obstructive sleep apnoea and the presence of left ventricular dysfunction. In addition, they showed that sustained daytime pulmonary hypertension in patients with obstructive sleep apnoea can be reversed after effective continuous positive airway pressure (CPAP) treatment. The strength of the study of Arias et al. is that their patients randomly received either sham or effective treatment with CPAP for 12 weeks and they could show that only effective treatment reduced pulmonary systolic pressure levels.

The study points out to an effective therapy to reduce the large burden of heart failure in these patients. In contrast, screening of heart failure patients for the presence of
obstructive sleep apnoea may uncover those patients who take advantage of effective CPAP treatment.

The potential mechanisms of daytime pulmonary hypertension in obstructive sleep apnoea are still under debate. Serum levels of vascular endothelial growth factor—a hypoxia-sensitive glycoprotein stimulating neoangiogenesis—are elevated in patients with obstructive sleep apnoea. It is assumed that the post-capillary component of daytime pulmonary hypertension is due to diastolic dysfunction and that the pre-capillary component results from repetitive hypoxia-reoxygenation during the night, leading to both pulmonary vasoconstriction and vascular endothelial remodelling. Furthermore, genetic factors seem to determine the link between hypoxia and the manifestation of pulmonary hypertension.

There are still unresolved questions: should all patients with obstructive sleep apnoea be screened for coexisting pulmonary hypertension, and should all obstructive sleep apnoea patients with pulmonary hypertension be treated with CPAP, even if they are not symptomatic with regard to daytime sleepiness? Nonetheless, the study by Arias et al.8 provides a new piece of the puzzle, showing that obstructive sleep apnoea is not only an underestimated cardiovascular risk factor, but that there is effective treatment with the chance of modifying the otherwise increased cardiovascular morbidity and mortality.

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References