

Association of Obstructive Sleep Apnea Syndrome (OSAS) and Nonalcoholic Steatohepatitis (NASH)

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Obstructive sleep apnea hypopnea syndrome (OSAS) is characterized by excessive daytime sleepiness and nighttime breathing cessation or reduction of airflow. OSAS is associated with significant morbidity and mortality. The prevalence of OSAS in community-screened patients is 2-14% [1]. OSAS is associated with hypertension, heart failure, cardiac arrhythmias, insulin intolerance and diabetes. Older age, hypertension, male sex and a BMI of greater than 31.4 are risk factors for OSAS [1].

Nonalcoholic steatohepatitis (NASH) is characterized by hepatocyte inflammation, necrosis and apoptosis, and varying degrees of fibrosis in the presence of lipid-laden hepatocytes. The prevalence of NASH is estimated to be 30% in the general population and more than 75% in obese patients with type 2 diabetes [2]. Visceral obesity is a major determinant for the development of NASH. Increased insulin resistance, enhanced lipolysis and free fatty acid release are considered to be the main pathogenic mechanism [2].

In this issue of the journal, Shigefuku et al. present a case of NASH in a patient with OSAS whose liver enzymes improved after continuous positive airway pressure (CPAP) treatment. An association of OSAS with NASH has recently been established. OSAS has been found to be a risk factor for liver injury independent of obesity [3]. Indeed, in a recent meta-analysis, odds ratio of OSAS for the presence of NASH was 2.37 [4].

In view of the possible beneficial effects of treatment of OSAS on progression of NASG, it has been suggested that patients with OSAS should be screened for the presence and severity of NASH. But the optimal method of screening is not yet clear. Elevation of alanine aminotransferases (ALT) is not sufficiently sensitive for detection of NASH and an imaging method like ultrasound in combination with liver enzymes may be more sensitive. Similarly, patients with NASH should be screened for the presence of OSAS. This may be done in two stages; a standard questionnaire should first assess the pre-test probability of the disease followed by overnight polysomnography in high risk patients

So what is the rationale behind the improvement in the liver enzyme levels due to CPAP therapy? Both diseases share certain risk factors for their development. Oxidative stress and obesity are thought to play a role in the pathogenesis of both OSAS and NASH. Obstructive sleep apnea also increases the risk of insulin resistance, which is thought to play a pathogenic role in the development of NASH. Chronic intermittent hypoxia of OSAS and inflammation as suggested by raised levels of IL-6 and TNF may also play a role in the pathogenesis of NASH. CPAP therapy may act by reducing oxidative stress, improving insulin resistance and other still undefined mechanisms. There is some evidence that CPAP therapy improves insulin resistance. In a meta-analysis by Yang et al. CPAP significantly improved insulin resistance in non-diabetic patients with moderate to severe OSA, while no significant change in body mass index was detected [5]. In another study, continuous positive airway pressure therapy has beneficial effects on vascular function and oxidative stress in patients with the metabolic syndrome and OSAS [6]. In view of the above studies, it is likely that the beneficial effects of CPAP therapy on liver enzymes in NASH is due to reduction in oxidative stress and possibly inflammatory cytokines but

further research is needed to elucidate the exact role of CPAP treatment in NASH and possibly diabetes mellitus. Long-term effects of CPAP on cardio-metabolic markers including insulin resistance require well-designed prospective studies.

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