

Metabolic Disorders in Obstructive Sleep Apnea

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Obstructive Sleep Apnea (OSA) is now recognized to be associated with several metabolic abnormalities. Obesity is a confounding factor for these perturbations, but it may also be a consequence of OSA [1].

Impaired Glucose Metabolism and OSA

It is now well established that OSA and impaired glucose metabolism [including insulin resistance, glucose intolerance and type 2 Diabetes Mellitus (DM)] may coexist. Cross-sectional studies have demonstrated that up to 30% of patients with OSA, diagnosed by polysomnography, have type 2 diabetes [2], while 86% of obese patients with type 2 diabetes have OSA [3]. However, due to confounding factors such as obesity, a causal relationship between OSA and impaired glucose metabolism has not been unequivocally shown. In a series of 2656 subjects enrolled in the Sleep Heart Health Study, elevated fasting glucose and 2-hour postprandial glucose levels were significantly higher in patients with moderate-to-severe OSA than in normal subjects [4]. Furthermore, Apnea Hypopnea Index (AHI) was independently associated with fasting and 2-hour postprandial glucose levels and with the degree of insulin resistance. In a cross-sectional analysis of participants without DM, AHI ≥ 10 was shown to correlate with glucose dysmetabolism [5].

The putative mechanisms underlying glucose dysmetabolism in OSA include chronic inflammation via activation of the Nuclear Factor κ B (NF- κ B) pathway, chronic intermittent hypoxia with resultant sympathetic over-activation and sleep fragmentation [1].

The effects of Continuous Positive Airway Pressure (CPAP) therapy on glucose alterations in OSA are uncertain, while there is a significant discrepancy between individual studies [6]. Indeed, some works have confirmed an improvement of glucose metabolism with CPAP therapy, including decrease in glucose levels and in HbA1c, improvement in insulin sensitivity, fasting insulin levels and insulin secretion. Nonetheless, others have yielded negative findings [6]. However, the latter are largely attributable to the impact of obesity, which may counterbalance the effect of treatment. Additionally, patient adherence to CPAP treatment is an important, often neglected, factor influencing outcomes [7].

Dyslipidemia and OSA

The association between OSA and dyslipidemia is still unclear. It has been suggested that chronic intermittent hypoxia in OSA is a risk factor for dyslipidemia. The Sleep Heart Health Study in men has demonstrated that total cholesterol levels were positively associated with Respiratory Disturbance Index (RDI), after adjusting for age and Body Mass Index (BMI) [8]. Furthermore, serum High-Density Lipoprotein Cholesterol (HDL-C) in women was inversely associated and triglycerides were positively associated with RDI [8]. Importantly, obesity alone does not explain the association between OSA and dyslipidemia. Moreover, Börgel et al. [9] showed a significant correlation between AHI and serum HDL-C levels in OSA patients, independently of age, sex, BMI, diabetes and lipid-lowering medication, while no independent associations were found with serum

levels of total cholesterol, triglycerides and Low-Density Lipoprotein Cholesterol (LDL-C) [9].

Some authors suggest that HDL-C may be dysfunctional in OSA patients, contributing to increased cardiovascular risk [10]. Still, due to the presence of confounders, such as obesity, the short duration of studies and the lack of controls, it remains to be determined whether OSA is a risk factor for dyslipidemia.

Of note, recent research has indicated that CPAP treatment may significantly increase serum HDL-C within 6 months [9]. An independent association was found between change in AHI and changes in HDL-C or triglyceride levels [9]. However, due to the paucity of evidence, the beneficial effect of CPAP therapy on serum lipids awaits further confirmation [11].

Metabolic Syndrome and OSA

Metabolic syndrome (MS) and OSA are commonly diagnosed in the same patient. It has been suggested that OSA is a further manifestation of the metabolic syndrome, and their coexistence has been named as "syndrome Z" [12]. The Wisconsin Sleep Cohort Study has demonstrated that there is a significant correlation between OSA and MS (diagnosed by the NCEP-ATP III definition) [13]. In a retrospective examination of 250 consecutive patients referred for the evaluation of OSA, the frequency of MS was significantly higher in those with OSA (60%) than those without OSA (40%) ($p=0.004$) [14].

Furthermore, recent studies have suggested that OSA has an additive effect on the development of atherosclerosis in MS patients. MS patients with moderate-to-severe OSA seem to have higher levels of carotid intima-media thickness, carotid-femoral pulse wave velocity and carotid artery diameter than those without or mild OSA [15].

In an observational study of patients with severe OSA and MS, CPAP therapy has been found to induce substantial improvements in patients with adequate treatment compliance [16]. Specifically, reductions in systolic and diastolic blood pressure, insulin resistance, systemic inflammation, oxidative stress and the global cardiovascular risk were seen [16]. Moreover, one trial has shown a significant reduction in the prevalence of MS following treatment of OSA [17]. In the light of this evidence, additional enquiry into the effect of CPAP on metabolic syndrome is warranted.

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References

1. Lévy P, Bonsignore MR, Eckel J (2009) Sleep, sleep-disordered breathing and metabolic consequences. *Eur Respir J* 34: 243-260.
2. Meslier N, Gagnadoux F, Giraud P, Person C, Ouksel H, et al. (2003) Impaired glucose-insulin metabolism in males with obstructive sleep apnoea syndrome. *Eur Respir J* 22: 156-160.
3. Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, et al. (2009) Obstructive sleep apnea among obese patients with type 2 diabetes. *Diabetes Care* 32: 1017-1019.
4. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, et al. (2004) Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. *Am J Epidemiol* 160: 521-530.
5. Seicean S, Kirchner HL, Gottlieb DJ, Punjabi NM, Resnick H, et al. (2008) Sleep-disordered breathing and impaired glucose metabolism in normal-weight and overweight/obese individuals: the Sleep Heart Health Study. *Diabetes Care* 31: 1001-1006.
6. Steiropoulos P, Papanas N, Nena E, Maltezos E, Bouros D (2010) Continuous positive airway pressure treatment in patients with sleep apnoea: does it really improve glucose metabolism? *Curr Diabetes Rev* 6: 156-166.
7. Steiropoulos P, Papanas N, Maltezos E, Bouros D (2009) Is there a metabolic effect of continuous positive airway pressure in sleep apnoea? Adherence should not be underestimated. *Eur Respir J* 34: 1209-1210.
8. Newman AB, Nieto FJ, Guidry U, Lind BK, Redline S, et al. (2001) Relation of sleep-disordered breathing to cardiovascular disease risk factors: the Sleep Heart Health Study. *Am J Epidemiol* 154: 50-59.
9. Börgel J, Sanner BM, Bittlinsky A, Keskin F, Bartels NK, et al. (2006) Obstructive sleep apnoea and its therapy influence high-density lipoprotein cholesterol serum levels. *Eur Respir J* 27: 121-127.
10. Tan KC, Chow WS, Lam JC, Lam B, Wong WK, et al. (2006) HDL dysfunction in obstructive sleep apnea. *Atherosclerosis* 184: 377-382.
11. Michailidis V, Steiropoulos P, Nena E, Papanas N, Maltezos E, et al. (2011) Continuous positive airway pressure treatment: effect on serum lipids in patients with obstructive sleep apnoea. *Open Cardiovasc Med J* 5: 231-238.
12. Wilcox I, McNamara SG, Collins FL, Grunstein RR, Sullivan CE (1998) "Syndrome Z": the interaction of sleep apnoea, vascular risk factors and heart disease. *Thorax* 53: S25-S28.
13. Nieto FJ, Peppard PE, Young TB (2009) Sleep disordered breathing and metabolic syndrome. *WMJ* 108: 263-265.
14. Parish JM, Adam T, Facchiano L (2007) Relationship of metabolic syndrome and obstructive sleep apnea. *J Clin Sleep Med* 3: 467-472.
15. Drager LF, Bortolotto LA, Maki-Nunes C, Trombetta IC, Alves MJ, et al. (2010) The incremental role of obstructive sleep apnoea on markers of atherosclerosis in patients with metabolic syndrome. *Atherosclerosis* 208: 490-495.
16. Dorkova Z, Petrasova D, Molcanyiova A, Popovnakova M, Tkacova R (2008) Effects of continuous positive airway pressure on cardiovascular risk profile in patients with severe obstructive sleep apnea and metabolic syndrome. *Chest* 134: 686-692.
17. Mota PC, Drummond M, Winck JC, Santos AC, Almeida J, et al. (2011) APAP impact on metabolic syndrome in obstructive sleep apnea patients. *Sleep Breath* 15: 665-672.