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Sleep Medicine 2 (2001) 161–163

SLEEP MEDICINE

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Journal search and commentary

Article reviewed: Serum leptin and vascular risk factors in obstructive sleep apnea ☆

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Accepted 13 December 2000

Objective

To characterize the profile of metabolic elements which may have implications for the cardiovascular risk associated with Obstructive Sleep Apnea-Hypopnea (OSA) as well as to quantify leptin before and after treatment with continuous positive airway pressure (CPAP).

Study design

Case-control study; hospital based sleep center.

Study population

Thirty OSA patients (Apnea + Hypopnea Index: 35.7 ± 18, mean ± SD) and 30 control subjects without OSA (Apnea + Hypopnea Index: 1.8 ± 1.9), but matched for age (OSA: 43.6 ± 10.1; no OSA: 41.9 ± 7.4), gender (each group: 27 men/three women), BMI (OSA: 27 ± 2.9; no OSA: 26.6 ± 2.1 and, when relevant, menopausal status.

Methods

In all study participants, anthropomorphic features, glucose, insulin, lipids and leptin were assessed and the two groups were compared at baseline. Blood was sampled between 08:00 and 09:00 h with individuals in a fasting state for an unspecified duration. Subsequently, measurements were made in seven OSA patients after an overnight trial of CPAP and in nine OSA patients after six months of CPAP therapy. No data relating to CPAP adherence was presented.

Results

Despite having comparable body mass index (BMI), neck, waist and hip circumference, the OSA group had more subcutaneous fat, measured by skinfold thickness than the non-OSA group. Diastolic but not systolic blood pressure was also higher in the OSA group (diastolic pressure: OSA, 81 ± 12; non-OSA 73 ± 12 mmHg). At baseline, insulin, insulin/glucose ratio, triglyceride, total cholesterol/ high density lipoprotein (HDL) cholesterol ratio and leptin levels were significantly greater in the OSA patients. Across all participants (OSA and non-OSA), variables which were independently correlated with serum leptin levels included skinfold thickness, waist/hip ratio, serum low density lipoproteins (LDL) cholesterol and diastolic blood pressure. Specifically in OSA patients, serum insulin and diastolic blood pressure were independently correlated with serum leptin.

☆ M.Sm. Ip, K.S.L. Lam, C. Ho, K.W.T. Tsang, W. Lam, (Chest 2000;118:580-586).

PII: S1389-9457(01)00074-0

After 6 months of CPAP therapy ($n = 9$ OSA patients), there was no significant change in BMI but there were significant reductions in serum leptin and triglyceride level The changes in anthropomorphic data between baseline and after 6 months of CPAP therapy were not presented.

Conclusion

The investigators concluded that elevated serum leptin levels in OSA are not explained by increased 'adiposity' and that increased leptin is a marker for OSA. The reduction in serum leptin with CPAP treatment of OSA suggests that there is a specific pathophysiologic process, such as increased sympathetic autonomic activity that is associated with OSA which increases leptin. The authors also conclude that there are specific lipid profiles in patients with OSA which may be associated with enhanced cardiovascular risk and are not explained simply by increased BMI.

Comment

There is increasing information becoming available regarding the metabolic effects of leptin as well as the implications of this protein on various physiologic functions. Leptin is produced by white adipose and placental tissue. It inhibits neuropeptide Y synthesis in the hypothalamus and down-regulates food intake. Leptin also is associated with increased energy expenditure. In genetically altered animal models of obesity-hypoventilation, leptin administration augments alveolar ventilation and prevents deleterious breathing patterns, independent of weight [1,2]. Leptin levels are generally high in obese subjects, consistent with an element of leptin-resistance. It is therefore perhaps not surprising that OSA patients have elevated serum leptin levels due to the association between this condition and obesity. In this regard, increased baseline leptin levels observed by Ip et al. in the OSA patients could be due to the increased sub-cutaneous fat in this group relative to the non-OSA subjects. Indeed, the distribution of adipose tissue, not the BMI may be relevant to leptin levels since leptin levels may correlate with sub-cutaneous but not visceral fat [3]. It is most interesting however, that Ip and coworkers confirmed the observation made by Chin et al. [3] that serum leptin levels decrease following a 3–4 days and also 6 months of CPAP therapy and that this occurs independent of any change in weight. In addition to the possibility that reduction of sympathetic nerve activity leads to reduced leptin levels [4], Chin et al. [3] suggested that CPAP may alter the clearance of leptin by virtue of changing cardiac output and regional abdominal perfusion.

The leptin story continues to evolve. At least one study has suggested that leptin may have therapeutic efficacy in the management of obesity [5] and if proven to be the case, would have major impact on how we treat OSA patients. At this time however, the research by Ip et al. and Chin et al. [3] suggests that if leptin resistance is a feature of obesity in OSA patients, it may be decreased by CPAP since body weight remains the same in the presence of lower levels. Another issue to consider however, is the observation by both groups of investigators as well as others [6] that many, if not most OSA patients do not lose weight following initiation of treatment. In this context, is it possible that an increase in leptin sensitivity, with associated promotion of weight reduction, is insufficient to off-set the decrease in leptin levels (serum, cerebrospinal fluid, hypothalamic tissue level or wherever the active site might be) such that weight reduction does not result. Alternatively, are there other, as yet unknown factors that contribute to maintenance of the obesity despite quantitative and functional changes in leptin?

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