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Journal search and commentary

Article reviewed: Sleep apnea and daytime sleepiness and fatigue: related to visceral obesity, insulin resistance, and hypercytokinemia[☆]

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Category

Sleep apnea, obesity

Objective(s)

Test the following three hypotheses:

(1) Sleep apnea independent of obesity contributes to increases in inflammatory plasma cytokines (tumor necrosis factor (TNFα) and interleukin-6 (IL-6)) and leptin;

(2) Visceral fat correlates more closely to sleep apnea than does subcutaneous (s.c.) or total fat;

(3) Sleep apnea independent of obesity contributes to the development of insulin resistance.

Study design

Between subject comparisons for three groups and also multiple regression analyses across and within the groups.

Study population

Males, 14 sleep apneics (average ± SE: age, 46.6 ± 3.0; BMI, 38.4 ± 1.6; A/HI, 48.7 ± 5.6), 11 obese controls (age, 40.2 ± 2.2; BMI, 36.2 ± 2.4; A/HI 1.3 ± 0.5), and 12 normal weight controls (age, 45.4 ± 2.8; BMI, 26.0 ± 0.8; A/HI, 0.5 ± 0.3) recruited from the sleep disorders clinic and through community advertisements. Subjects diagnosed with diabetes were excluded from the study.

Methods

After one screening night polysomnogram (PSG) all participants had a PSG for 4 consecutive nights (first night for adaptation). Air flow was measured using thermocouples at the nose and mouth. Blood samples to measure TNFα, IL-6, and leptin were obtained from all subjects for 3 consecutive days at 06:00–07:00 after the PSG and again at 19:00–20:00. Blood samples were also obtained in the same mornings for fasting glucose and insulin for both obese groups only. Computed tomographic (CT) scanning using axial 8-mm slices through mid-vertebral bodies (L1–L5) plus a 5th scan atop the femoral heads was used to measure total, s.c. and visceral fat.

[☆] Vogonttzas AN, Papanicolaou DA, Bixler EO, Hopper K, Lotsikas A, Lin HM, Kales A, Chrousos GP. Sleep apnea and daytime sleepiness and fatigue: related to visceral obesity, insulin resistance, and hypercytokinemia. J Clin Endocrin Metab 2000;85:1151–1158.

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Results

Sleep apnea patients compared to the other two groups showed higher blood pressure and significantly poorer sleep with reduced sleep efficiency and longer sleep latency. TNFα, IL-6 and leptin correlated significantly with BMI and A/HI and were significantly increased for apnea patients compared to normal weight controls. The obese controls had values between these groups but the differences were not statistically significant ($P > 0.05$) except for leptin. The leptin values were significantly greater for apneics than for obese controls. The normal circadian pattern of TNFα, IL-6 and leptin with greater values in the morning than evening were significantly altered being reduced for TNFα and actually reversed for IL-6 and leptin.

Sleep apneics compared to obese controls showed significantly greater fasting blood glucose (average ± SE: 106.2 ± 4.1 vs. 85.4 ± 4.4 μg/dl, $P < 0.01$) and higher plasma insulin levels (25.7 ± 4.2 vs. 14.6 ± 2.5 μg/dl, $P < 0.05$). Sleep apneics compared to obese controls also showed on the CT scans significantly greater visceral fat areas but no significant difference for total body fat or s.c. fat areas. Visceral fat but not total or s.c. fat correlated significantly with A/HI.

Multivariate analyses with both types of fat and A/HI as independent variables showed that A/HI provided an independent significant contribution to prediction of IL-6 and TNFα but not to leptin.

Conclusion

The authors concluded that sleep apnea independent of obesity contributes to increased TNFα, IL-6 and leptin and to the development of insulin resistance. They further conclude that visceral obesity is a more significant contributing factor for sleep apnea than generalized obesity.

Comment

These data provide further evidence of the nature of the sleep apnea relationship to diabetes and abnormal elevations in the cytokines and leptin. It is particularly striking that apnea condition independent of the general obesity contributes to these abnormalities. The significance of visceral obesity for apnea and particularly for the leptin levels deserves further study. This central obesity with visceral fat has been associated with diabetes, hypertension, and also with increased lipids and cardiovascular disease. These data suggest this is also the primary fat problem for sleep apnea.

Even controlling for the effects of visceral fat it appears that the A/HI continues to have some added effect on the cytokines by a mechanism still not understood, possibly by disruption of the circadian patterns or producing nocturnal elevations of hormones. Unfortunately the results from a similar multivariate analyses for glucose or insulin were not reported.

The one, somewhat unusual aspect of these data is the significantly long sleep latency for the sleep apneics compared to either the obese or normal weight controls. Most sleep apneics have a marked problem with sleepiness and have short initial sleep latency. They often have interrupted sleep and sometimes reduced sleep efficiency, but it is rare that they do not fall asleep quickly in almost any situation. This would suggest that despite the apnea rates reported here these patients may not have been very severely affected by their apnea disorder, or that they experienced greater stress disturbing sleep onset than did other patients. Aside from this one concern these data strongly support the view that the medical problems associated with sleep apnea result from both visceral obesity and some other factor. One other factor may be the sleep loss experienced by these patients since this has recently been found to increase insulin resistance in normal subjects. Clearly sleep apnea is more than its associated obesity.