Journal Scan

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Indian J Sleep Med 2011; 6.1, 30-34

Sleep Breath - 01-SEP-2010; 14(3): 261-9

Inflammation accelerates atherosclerotic processes in obstructive sleep apnea syndrome (OSAS) - Quercioli A

Obstructive sleep apnea syndrome (OSAS) is an often underestimated sleep disorder that has been associated with cardiovascular disease. OSAS is characterized by cycles of apnea and/or hypopnea during sleep caused by the collapse of the upper airways. Intermittent hypoxia deriving from the cycles of apnea/arousals (to retrieve the ventilation) plays a pivotal role in the pathogenesis of the disease. Obesity is the most frequent predisposing condition of OSAS. Recent evidence suggests that OSAS could be considered as a pro-atherosclerotic disease, independently of visceral fat amount. Oxidative stress, cardiovascular inflammation, endothelial dysfunction, and metabolic abnormalities in OSAS could accelerate atherogenesis. The present review is focused on the possible pathophysiological mediators which could favor atherosclerosis in OSAS.

Best Pract Res Clin Endocrinol Metab - 01-OCT-2010; 24(5): 775-84

Sleep loss and inflammation

Mullington JM

Controlled, experimental studies on the effects of acute sleep loss in humans have shown that mediators of inflammation are altered by sleep loss. Elevations in these mediators have been found to occur in healthy, rigorously screened individuals undergoing experimental vigils of more than 24h, and have also been seen in response to various durations of sleep restricted to between 25 and 50% of a normal 8h sleep amount. While these altered profiles represent small changes, such sub-clinical shifts in basal inflammatory cytokines are known to be associated with the future development of metabolic syndrome disease in healthy, asymptomatic individuals. Although the mechanism of this altered inflammatory status in humans undergoing experimental sleep loss is unknown, it is likely that autonomic activation and metabolic changes play key roles.

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Brain Behav Immun - 01-JAN-2010; 24(1): 54-7

Sleep loss activates cellular markers of inflammation: sex differences

Irwin MR

ABSTRACT: Sleep disturbance is associated with inflammation and related disorders including cardiovascular disease, arthritis, and diabetes mellitus. Given sex differences in the prevalence of inflammatory disorders with stronger associations in females, this study was undertaken to test the effects of sleep loss on cellular mechanisms that contribute to proinflammatory cytokine activity. In 26 healthy adults (11 females; 15 males), monocyte intracellular proinflammatory cytokine production was repeatedly assessed at 08:00, 12:00, 16:00, 20:00, and 23:00h during a baseline period and after partial sleep deprivation (awake from 23:00 to 3.00h). In the morning after a night of sleep loss, monocyte production of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha) differentially changed between the two sexes. Whereas both females and males showed a marked increase in the lipopolysaccharide

(LPS) - stimulated production of IL-6 and TNF-alpha in the morning immediately after PSD, production of these cytokines during the early- and late evening was increased in the females as compared to decreases in the males. Sleep loss induces a functional alteration of monocyte proinflammatory cytokine responses with females showing greater cellular immune activation as compared to changes in males. These results have implications for understanding the role of sleep disturbance in the differential risk profile for inflammatory disorders between the sexes.

Transl Res - 01-JAN-2010; 155(1): 35-43

Systemic and airway inflammation in sleep apnea and obesity: the role of ICAM-1 and IL-8.

Carpagnano GE

ABSTRACT: The recurrent hypoxic stress that characterizes obstructive sleep apnea (OSA) seems to play a role in the increased adherence of neutrophils to endothelial cells as well as in the resulting migration of the former to the inflamed area. Intercellular adhesion molecule 1 (ICAM-1) and interleukin (IL)-8 are markers widely used in OSA studies to investigate inflammation. The aim of this study was to measure ICAM-1 and IL-8 levels in the breath condensate and in the plasma and inflammatory cells in the induced sputum of 12 obese OSA (OO) patients, 10 nonobese OSA (NOO) patients, 10 obese non-OSA (ONO) subjects, and 8 healthy subjects (HS) using a specific enzyme immunoassay (EIA) kit. A significant increase in both plasma and exhaled IL-8 and ICAM concentrations and percentage neutrophils was observed in the induced sputum of obese OSA patients, non-obese OSA patients, and obese non-OSA subjects compared with healthy subjects. However, although these inflammatory markers were found to follow an upward trend in obese OSA patients no difference was observed in both either non-obese OSA patients and obese non-OSA subjects. Finally, a significant positive correlation was found to occur among IL-8, ICAM-1, and sputum neutrophils, as well as across the apnea-hypopnoea index (AHI), TST 90%, body mass index (BMI), and neck circumference. The data obtained confirm the occurrence of an ICAM- and IL-8-mediated neutrophilic airway inflammation in both OSA and obese patients. The degree of inflammation, which seems to worsen in cases of comorbidity (OSA and obesity), is likely to be responsible for the increased risk of developing cardiovascular events observed in these subjects, and therefore, it deserves to be elucidated even more.

Pediatr Pulmonol - 01-JUL-2010; 45(7): 693-9

Adiposity and low-grade systemic inflammation modulate matrix metalloproteinase-9 levels in Greek children with sleep apnea.

Kaditis AG

BACKGROUND: Matrix metalloproteinase-9 (MMP-9) plasma levels correlate with C-reactive protein (CRP) concentrations and they are both increased in adults with obstructive sleep apnea (OSA). No studies have evaluated MMP-9 levels in children with sleep apnea and CRP is not consistently elevated in pediatric OSA. The aim of this investigation was to evaluate the association of severity of OSA, adiposity, and CRP with MMP-9 plasma levels in Greek children.

METHODS: Consecutive children with snoring who underwent polysomnography and were found to have OSA (obstructive apnea-hypopnea index-OAHI > or = 1 episode/hr) were recruited. Subjects without OSA (OAHI < 1 episode/hr) were included for comparison. Morning plasma MMP-9 and CRP were measured.

RESULTS: Twenty-nine children with moderate-to-severe OSA (age 5.4 +/- 1.5 years; OAHI 13.9 +/- 13.0 episodes/hr), 55 participants with mild OSA (6.4 +/- 2.6 years; OAHI 2.4 +/- 1.1 episodes/hr) and 22 subjects without OSA (6.8 +/- 2.6 years; OAHI 0.6 +/- 0.2 episodes/hr) were studied. Children with moderate-to-severe OSA were similar to those with mild OSA or without OSA regarding ln-transformed MMP-9 values (5.87 +/- 0.60 vs. 5.84 +/- 0.55 vs. 5.80 +/- 0.46; P > 0.05) and CRP concentrations (0.22 +/- 0.29 mg/dl vs. 0.21 +/- 0.36 vs. 0.13 +/- 0.16 mg/dl; P > 0.05). In multiple linear regression, body mass index (P = 0.027) and CRP levels (P = 0.008), but not OAHI or SpO(2) nadir (P > 0.05), were significantly related to MMP-9 values.

CONCLUSIONS: Adiposity and systemic inflammation unrelated to OSA severity, modulate MMP-9 levels in Greek children.

Lipids Health Dis - 01-JAN-2010; 9: 125

Sleep deprivation affects inflammatory marker expression in adipose tissue.

Rosa Neto JC

Sleep deprivation has been shown to increase inflammatory markers in rat sera and peripheral blood mononuclear cells. Inflammation is a condition associated with pathologies such as obesity, cancer, and cardiovascular diseases. We investigated changes in the pro and anti-inflammatory cytokines and adipokines in different depots of white adipose tissue in rats. We also assessed lipid profiles and serum levels of corticosterone, leptin, and adiponectin after 96 hours of sleep deprivation.

METHODS: The study consisted of two groups: a control (C) group and a paradoxical sleep deprivation by 96 h (PSD) group. Ten rats were randomly assigned to either the control group (C) or the PSD. Mesenteric (MEAT) and retroperitoneal (RPAT) adipose tissue, liver and serum were collected following completion of the PSD protocol. Levels of interleukin (IL)-6, interleukin (IL)-10 and tumour necrosis factor (TNF)-Î± were analysed in MEAT and RPAT, and leptin, adiponectin, glucose, corticosterone and lipid profile levels were analysed in serum.

RESULTS: IL-6 levels were elevated in RPAT but remained unchanged in MEAT after PSD. IL-10 protein concentration was not altered in either depot, and TNF-Î± levels decreased in MEAT. Glucose, triglycerides (TG), VLDL and leptin decreased in serum after 96 hours of PSD; adiponectin was not altered and corticosterone was increased.

CONCLUSIONS: PSD decreased fat mass and may modulate the cytokine content in different depots of adipose tissue. The inflammatory response was diminished in both depots of adipose tissue, with increased IL-6 levels in RPAT and decreased TNF-Î ± protein concentrations in MEAT and increased levels of corticosterone in serum.

Chest - 01-SEP-2010; 138(3): 528-35

B-type natriuretic peptide and cardiovascular function in young children with obstructive sleep apnea.

Goldbart AD

ABSTRACT

OBJECTIVE: N-terminal pro-B-type natriuretic peptide (NT-proBNP), a marker of ventricular strain, and C-reactive protein (CRP), a marker of inflammation, are reportedly elevated in school-aged children with obstructive sleep apnea (OSA). We hypothesized that cardiovascular morbidity affects circulating markers and their echocardiographic and polysomnographic (PSG) correlates in young children with OSA.

METHODS: We assessed young children undergoing adenotonsillectomy (TA) for OSA by polysomnography, echocardiography, and serum CRP and NT-proBNP levels.

RESULTS: A total of 90 children with OSA (mean age 19 +/- 7 months; 71.2% male; BMI, z = 0.62 +/- 1.04) and 45 age- and sex-matched controls were included. Three months following TA, 72 children were reassessed for NT-proBNP and CRP. NT-proBNP level (pg/mL) was higher in subjects with OSA (189.1 +/- 112.7) vs control subjects (104.8 +/- 49.5; P = .006). Both NT-proBNP (187.8 +/- 114 vs 86 +/- 32.6; P = .002) and CRP levels (mg %) (0.49 +/- 0.41 vs 0.1 +/- 0.17; P < .05) decreased following TA. Doppler pulse wave measuring tricuspid regurgitation (TR), a reflection of pulmonary hypertension, correlated with CRP (r = 0.61, P < .01) but not NT-proBNP (r = -0.14, P = .53) levels. Left ventricle end-diastolic diameter (LVEDD) was at the maximal normal range (0.91 +/- 0.11), but did not correlate with CRP or NT-proBNP levels. Both CRP level and TR correlated with PSG variables reflecting nocturnal hypoxemia, whereas NT-proBNP level and LVEDD did not. Echocardiography in 40 children (out of 90) showed a decline in TR that was abnormal before TA and correlated with the decrease in CRP following TA.

CONCLUSIONS: NT-proBNP levels are increased in children with OSA and decrease following TA. Echocardiographic parameters suggesting increased pulmonary pressure in young children with OSA are

related to nocturnal hypoxemia and systemic inflammation, which also decrease following therapy.

Circulation - 2-MAR-2010; 121(8): 1014-21

Vascular inflammation in obesity and sleep apnea.

Jelic S

BACKGROUND: Unrecognized obstructive sleep apnea (OSA) is highly prevalent in obesity. Both obesity and OSA are associated with vascular endothelial inflammation and increased risk for cardiovascular diseases. We investigated directly whether the endothelial alterations that are attributed commonly to obesity are in fact related to OSA.

METHODS AND RESULTS: Seventy-one subjects with a body mass index ranging from normal to obese underwent attended polysomnography. To assess vascular inflammation and oxidative stress directly, we quantified the expression of nuclear factor-kappaB and nitrotyrosine by immunofluorescence in freshly harvested venous endothelial cells. To evaluate basal endothelial nitric oxide (NO) production and activity, we quantified the expression of endothelial NO synthase (eNOS) and phosphorylated eNOS. Vascular reactivity was measured by brachial artery flow-mediated dilation. Expression of eNOS and phosphorylated eNOS and flow-mediated dilation were significantly lower, whereas expression of nitrotyrosine was significantly greater in OSA patients (n=38) than in OSA-free subjects (n=33) regardless of central adiposity. Expression of nuclear factor-kappaB was greater in obese OSA patients than in obese OSA-free subjects (P=0.004). Protein expression and flow-mediated dilation were not significantly affected by increasing body mass index or central obesity in OSA patients and in OSA-free subjects. After 4 weeks of continuous positive airway pressure therapy, flow-mediated dilation and expression of eNOS and phosphorylated eNOS significantly increased whereas expression of nitrotyrosine and nuclear factor-kappaB significantly decreased in OSA patients who adhered to continuous positive airway pressure > /= 4 hours daily.

CONCLUSIONS: Untreated OSA rather than obesity is a major determinant of vascular endothelial dysfunction, inflammation, and elevated oxidative stress in obese patients.

J Sleep Res - 01-JUN-2010; 19(2):341

The activation of the inflammatory cytokines in overweight patients with mild obstructive sleep apnoea.

Sahlman J

It is widely accepted that obstructive sleep apnoea (OSA) is linked with cardiovascular diseases. The relationship is complex and remains still poorly understood. The presence of chronic systemic inflammation has been connected with pathogenesis of both OSA and cardiovascular diseases. While atherogenesis is believed to be a process of many years, little is known about the potential impact of the largest OSA subgroup, mild OSA, on the development of cardiovascular diseases. The aim of the present study was to assess whether untreated mild OSA is associated with an activation of inflammatory cytokine system. The adult study population consisted of two groups: 84 patients with mild OSA [apnoea-hypopnoea index (AHI) 5-15 h(-1)] and 40 controls (AHI <5 h(-1)). Serum concentrations of pro- and anti-inflammatory cytokines were measured before any interventions. After adjustments for age, sex, body mass index, fat percentage, most important cardiometabolic and inflammatory diseases, and non-steroidal anti-inflammatory medication, the mean level of tumour necrosis factor-alpha was significantly elevated (1.54 versus 1.17 pg mL (-1), P = 0.004), whereas the level of interleukin-1 beta (IL-1 beta) was reduced (0.19 versus 0.23 pg mL(-1), P = 0.004) in patients with mild OSA compared with controls. The concentrations of the protective anti-inflammatory cytokines, interleukin-10 (1.28 versus 0.70 pg mL(-1), P < 0.001) and interleukin-1 receptor antagonist (478 versus 330 pg mL(-1), P = 0.003) were elevated in the OSA group. The concentrations of C-reactive protein increased, but IL-1 beta decreased along with the increase of AHI. Mild OSA was found to be associated not only with the activation of the pro-inflammatory, but also with the anti-inflammatory systems

Sleep Med Rev - 01-APR-2010; 14(2): 107-14

Sleep deprivation during pregnancy and maternal and fetal outcomes: is there a relationship?

Chang JJ

Sleep duration in the population has been declining. Women occupy an increasingly prominent place in the work force without reducing most of their responsibilities at home. Consequently, sleep needs are often pushed to the bottom of women's daily priority list. Prior research has indicated that sleep deprivation is associated with higher levels of pro-inflammatory serum cytokines. This is important because higher plasma concentrations of pro-inflammatory serum cytokine levels are associated with postpartum depression and adverse birth outcomes such as preterm delivery. However, little research has directly examined how sleep deprivation may affect maternal and fetal outcomes. This review summarizes the existing data on the effect of sleep deprivation during pregnancy on maternal and fetal outcomes. We review supporting evidence for the hypotheses that sleep deprivation during pregnancy increases the risk of preterm delivery and postpartum depression, and that systemic inflammation is the causal mechanism in the association. Prior research on sleep in pregnancy has been limited by varying data collection methods, subjective self-reported sleep measures, small and non-representative samples, cross-sectional designs; descriptive or non-hypothesis driven studies. Future research with longitudinal study designs is needed to allow examination of the effect of sleep deprivation on adverse maternal and fetal outcomes.

Sleep - 01-DEC-2010; 33(12): 1649-55

Are inflammatory and coagulation biomarkers related to sleep characteristics in mid-life women?: Study of Women's Health across the Nation sleep study.

Matthews KA

STUDY OBJECTIVES: Inflammation and pro-coagulation biomarkers may be a link between sleep characteristics and risk for cardiometabolic disorders. We tested the hypothesis that worse sleep characteristics would be associated with C-reactive protein (CRP), fibrinogen, factor VIIc, and plasminogen activator inhibitor (PAI)-1 in a multi-ethnic subsample of mid-life women enrolled in the Study of Women's Health across the Nation.

DESIGN: Cross-sectional.

MEASUREMENTS AND RESULTS: African American, Chinese, and Caucasian women (N=340) participated in 3 days of in-home polysomnographic (PSG) monitoring and had measures of inflammation and coagulation. Regression analyses revealed that each of the biomarkers were associated with indicators of sleep disordered breathing after adjusting for age, duration between sleep study and blood draw, site, menopausal status, ethnicity, residualized body mass index, smoking status, and medications that affect sleep or biomarkers. Among African American women, those who had higher levels of CRP had shorter PSG-sleep duration and those who had higher levels of fibrinogen had less efficient sleep in multivariate models.

CONCLUSIONS: These results suggest that inflammation and pro-coagulation processes may be an important pathway connecting sleep disordered breathing and cardiometabolic disorders in women of these ethnic groups and that inflammation may be a particularly important pathway in African Americans.