331. Obstructive sleep apnea: inflammation and metabolism

**P3044**

Markers of liver dysfunction in patients with obstructive sleep apnea
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Increased serum levels of liver enzymes have been reported in patients with obstructive sleep apnea (OSA), but the prevalence of liver dysfunction in OSA is poorly defined. In 91 consecutive patients (23 females) without serological evidence of viral hepatitis or alcohol-induced liver disease who underwent nocturnal respiratory monitoring for diagnosis of OSA, we measured alanine (ALT) and aspartate (AST) aminotransferase, and gamma-glutamyl transpeptidase (GGT) in serum, together with the HOMA Index and the lipid profile. Mean age and BMI were 55±4 years and 28,7±4 kg/m², mean AHI 49±22.8/hour. OSA was diagnosed with full polysomnography. In the study group patients 8 (45%) diagnosed with mild OSA, 10 patients (26.7%) moderate OSA and 46 patients (64.8%) severe OSA. Control group consisted of 18 subjects with excluded OSA, mean age 43±13 years, mean BMI 28,7±4 kg/m². Mean BMI 28,7±4 kg/m². In the study group the mean BMI was 68±4.1. 2.1. In the study group and control group circadian profile of melatonin secretion was assessed with radioimmunoassay method (RIA) at 6 time points.

**Results:** Melatonin concentration (pg/ml) at 0,00, 6,00, 10,00 am and 2,00, 6,00, 10,00 pm were: in the study group 91±807.6, 63,±548.8, 21,4±11.3, 17.9±3.3, 21,1±16.2, 50,1±40.6, and in the control group 136,7±93.9, 94,2±7,55, 30,4±29.5, 13.9±6.1, 16,5±11.9, 43,6±2.76 respectively. In the study group mean concentration of melatonin at 2.00 am and 6.00 am was significantly lower than in the control group, p=0,04 and p=0,02 respectively.

**Conclusion:** Patients with OSA has preserved circadian rhythm of melatonin secretion, with peak secretion at night hours. The maximum concentration of melatonin at night is significantly lower than in the healthy group.

**P3046**

Albuminuria in children with obstructive sleep apnea
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Increased excretion of albumin in urine has been considered a surrogate marker of endothelial dysfunction in adults with obstructive sleep apnea (OSA). Aim of this study was to evaluate urinary excretion of albumin in children with OSA.

**Methods:** Albumin-to-creatinine ratio (ACR) was calculated in a morning urine specimen collected from children with or without OSA. An assay appropriate for detection of microalbuminuria was used.

**Results:** Twenty seven subjects with moderate-to-severe OSA (5.6±2.1 y.o.; AHI 9.1±3.7 episodes/h), 71 subjects with mild OSA (6.2±2.3 y.o.; 2.4±1 episodes/h) and 31 children without habitual snoring (6.7±2.4 y.o.; 0.6±0.3 episodes/h) were studied. Subjects with moderate-to-severe OSA had similar ACR to those with mild OSA (p=0.072) and significantly higher ACR relative to subjects without habitual snoring (p=0.007): median 0.38 (0-14.3) mg/g vs. 0.31 (0-13) vs.0 (0-3.26), respectively. There was significantly increased risk for having ACR >20 in children with moderate-to-severe or mild OSA compared to children without habitual snoring after adjustment for age and gender: OR (95% CI) 6.4 (1.8-23.3) of 7 (1.6-69) vs. 1.0.

**Conclusions:** Children with OSA are at increased risk for having detectable morning albuminuria.

**P3047**

Biochemical basis of inflammation in children with obstructive sleep apnea syndrome (OSAS) and in children with obesity
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**Rationale:** OSAS and obesity are two risk factors that can lead to the early development of cardiovascular events very often coexisting, and it’s hard to understand the mechanisms that characterize each one. Our aim was to determine the different pathways of these two disorders.

**Methods:** We evaluated 38 children (24 female; age median: 7.68±3.78 years), divided in three groups (18 children with OSAS but non obese, 10 Obese children but without OSA, 10 controls). All children underwent blood sample test for the evaluation of CRP, hs, the lipidic and metabolic aspect (Glycemia, Insulin, Cholesterol total, LDL, and HDL, triglycerides, leptin, adiponectin, and resistin), the interleukines pattern (IL-1 α, β, IL-2, IL-4, IL-6, IL-10, IFN-γ, TNF-α, VEGF, EGF, MCP1) and the polysomnography examination.

**Results:** Children with OSAS and children with obesity showed higher levels of LDL-cholesterol and triglycerides compared to controls (OSAS p=0.005 and p=0.01; Obese p=0.01 and p=0.005). In the obese group leptin levels were significantly higher compared to controls and to the OSAS (p=0.00). In the OSAS groups we found significantly higher levels of IL-1 β (p=0.04) and TNF-α (p=0.05) compared to controls and obese groups.

**Conclusions:** OSAS and obesity have two different pathways. OSAS promotes an inflammatory pattern through the stimulation of TNF-α, whereas obesity determines an hormonal deregulation especially of the adipokines one, as leptin.
Antifluorinflammatory medications administered to children with obstructive sleep apnea (OSA) decrease size of pharyngeal lymphoid tissue and severity of airflow limitation. This study was designed to evaluate the effects of consensus subpopulations of tonsillar lymphocytes with potential susceptibility to inhibitors of cysteinyl leukotriene receptors.

Methods: Tonsillar tissue excised from children with OSA or controls with recurrent tonsillitis (RT) was studied for expression of types 1 and 2 cysteinyl leukotriene receptors (LT1R and LT2R) by immunofluorescence and flow cytometry.

Results: Ten children with moderate-to-severe OSA (age 5.8±3.3 years) and 10 subjects with RT (7.5±4.7 years) were studied. In both children with OSA and RT, immunoreactivity for LT1R and LT2R was detected in CD3+ tonsil T lymphocytes (extracellular areas) and in CD19+ B lymphocytes (germinal centers and mantle/marginal zones). In subjects with OSA, LT1R+ fraction of small size CD19+ B lymphocytes (median 26.4%, range 4.7%-77.7%) was significantly higher than the LT1R+ fraction of large size CD19+ B lymphocytes (3.3%, 1%-31.9%) (p=0.05 and p<0.05). Similar trend was identified for LT2R in children with OSA or RT and for LT1R in participants with RT.

Conclusions: Children with OSA or RT and tonsillar hypertrophy express cysteinyl leukotriene receptors in B lymphocytes of the tonsillar germinal centers and mantle/marginal zones and in extracellular T lymphocytes. These findings explain the beneficial effects of cysteinyl leukotriene inhibitor receptors on pharyngeal lymphoid tissue hypertrophy and OSA.
Aim: In this study we focused on the effects of weight loss and SDB on common metabolic parameters.

Methods: Consecutive obese children between 10 and 18 years were recruited. They followed a treatment program with diet, increased physical activity and psychological support. All children underwent a baseline sleep screening and a control study after 4-6 months of treatment in case of diagnosed SDB. A fasting blood assay was performed baseline and after 4-6 months.

Results: 84 children and adolescents with a median age of 15.1 years (9.5-18.9) were included. Mean BMI z-score was 2.73±0.41. 44% of the subjects had SDB, with obstructive sleep apnea (OSA) diagnosed with HDL-cholesterol ≤ 0.34 (P<0.002), ASAT (r=0.33, P<0.003) and ALAT (r=0.35; P<0.001). No correlations were found for glucose, triglycerides and total cholesterol. After weight loss treatment all metabolic parameters improved and only 8% of the patients had residual SDB. Improvements in ASAT and ALAT were mediated by improvements in BMI. Improvements in oxygen desaturation index (ODI) were associated with an increase in HDL-cholesterol (r=0.49; P<0.003).

Conclusions: This study confirms the link between ASAT, ALAT, HDL-cholesterol and SDB baseline. HDL-cholesterol improved after weight loss in association with improvements in ODI.

P3054

The impact of sleep apnea on glucose metabolism. Results from a long-time follow-up

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Background: It has been suggested that sleep-disordered breathing (SDB) is a risk factor for diabetes, but long-term follow-ups are lacking.

Objectives: To analyze the influence of SDB on future glucose metabolism.

Methods: Men without diabetes (n=141) were investigated with whole-night respiratory monitoring. After a mean period of 11.3 years, they were followed up with an interview, blood sampling and anthropometric measurements. Insulin resistance was quantified using the homeostasis model assessment (HOMA). Delta-HOMA-IR was calculated as the minimal nocturnal O2 saturation (90%) minus HOMA-IRbaseline. An oral glucose tolerance test was performed in 113 men to calculate the insulin sensitivity index. Confounders adjusted for were age, BMI, weight gain, hypertension, treatment for diabetes and years with CPAP during the period.

Main results: At the follow-up, 23 men had SDB. An apnea-hypopnea index (AHI) >5 and an oxygen desaturation index (ODI) >5 were significant predictors of developing diabetes. After adjusting for confounders, the association with ODI remained significant (adj OR 4.4, 95% CI 1.1-18.1). The ODI at baseline was inversely related to the insulin sensitivity index at the follow-up (r=-0.27, P=0.003). A deterioration in HOMA-IR was significantly related to all measured variables of sleep-disordered breathing (AHI, AHI, ODI, ODI and MiniSaO2) even when adjusting for confounders. When excluding the variable “years on CPAP” from the multivariate model, all associations weakened.

Conclusions: SDB is independently related to the development of insulin resistance and thereby the risk of diabetes mellitus. The results indicate that CPAP treatment can modify this risk.

P3065

Coronary plaque distribution and endothelial dysfunction in younger obstructive sleep apnea patients

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Background: Obstructive sleep apnea syndrome (OSA) influences endothelial function and causes cardiovascular diseases. Objectives: To assess the prevalence of endothelial dysfunction in patients with OSA.

Methods: Twenty-seven obese patients with OSA and 26 healthy obese subjects were investigated. The presence or absence of OSA was evaluated with a sleep study. Endothelial function was investigated with brachial artery ultrasound examination.

Results: Baseline characteristics were equivalent between the two groups. Minimal SaO2 and AHI in the OSA and control groups were [72.1±11.6 versus 86.5±4.5% (P=0.0001), and 27.9±23.1 versus 2.0±1.5 (P<0.001). There was no statistically significant difference in percentage change 2 of BADSLnitrate between patients and control groups (P=0.05) i.e. endothelial independent dilatation. Flow-mediated dilatation (FMD) percentage change 1 was highly significantly lower in OSA patients in comparison to control group [(Mean ± SD: 3.1±2.8 vs 10.6±6.9, (P=0.005) respectively i.e. endothelial dysfunction. There was positive significant statistical correlation between BMI and BAD and BADsl nitrate (r=-0.34; P=0.0005) and AHI in the time in which O2 saturation <90%, BAdFMD and BADsl among the patients with OSA, but there was negative significant correlation between BADsl and AHI in the time in which O2 saturation <90% (r=0.35; P=0.005).

Conclusions: We detected a prominent deterioration in endothelial function in obese OSA patients compared with healthy obese subjects. This deterioration may occur due to ongoing hypoxemia and it may be a possible cause of cardiovascular diseases in patients with OSA.
which might contribute to the onset of some of the systemic co-morbidities. Repeated hypoxia/re-oxygenation cycles may cause increase in Reactive Oxygen Species (ROS) with a reduction of Nitric Oxide (NO) availability.

This study was undertaken to assess oxidative stress in patients with severe OSAS (Apnea-Hypopnea index > 30/h) by evaluation of brachial artery Flow mediated dilation (FMD), gp91phox and serum levels of nitrite and nitrates (NOx), and to test the hypothesis that Continuous Positive Airway Pressure (CPAP) therapy can reduce oxidative stress.

We choose FMD as indirect marker of endothelial NO-mediated reactivity; gp91phox for NADPH oxidase activity and serum levels of NOx, markers of nitric oxide generation.

We enrolled 10 patients with severe OSAS. After polysomnography, for evaluation AHI and oxygen desaturation index (ODI), FMD, gp91phox and NOx were measured before and after 90 days of CPAP treatment. None of the patients smoked. The mean AHI and ODI prior to CPAP were respectively 43.3±11.9/h and 35.8±22.3/h, which decreased to 7.±5/h and 2.±1.6/h (p<0.001). The mean BMI was 35.±5.5 kg/m² and it didn’t change during 90 days of therapy. Gp91phox decreased from 32.±7.4 to 23.±5.1 (p<0.001).

FMD and NOx were not statistically significant.

While confirming the association between OSAS and oxidative stress, we found CPAP therapy managed to reduce gp91phox in patients who adhered to treatment for at least 4 hours daily, for 90 days, although there was no significant change in body weight.

CPAP treatment could therefore decrease Oxidative stress in patients with OSAS by correction of apnea and restoring normal oxygenation.

P3060
Is substance P (SP) involved in sleep physiology and behavioural characteristics in children with obstructive sleep apnea-hypopnea syndrome during sleep (OSAHS)?

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The neuropeptide substance P (SP) has been supposed to mediate sleep physiology and influence behavioral and cognitive functions. Its levels are found to be significantly lowered in patients with OSAHS.

This study aimed to measure SP levels1 in serum of children with OSAHS and to correlate them with sleep physiology and possible behavioural problems. 40 children were evaluated with overnight polysomnography for OSAHS. A questionnaire concerning the presence of aggressiveness, hyper-mobility, attention deficit disorders and behaviour problems was fulfilled. Relationship between serum SP levels and number of total apneas, respiratory events, REM/non-REM sleep were calculated using Pearson correlation analysis; p < 0.05 was considered statistically significant.

14/40 children had mild, 14/40 moderate and 12/40 severe degree of OSAHS. In 25/40 (62.5%) children low levels of SP were recorded (314.36±58.32), and the rest 15/40 (37.5%) had normal values (538.51±58.32) and the rest 15/40 (37.5%) had normal values (538.51±58.32). No statistical significance was found between SP levels and: a) stage 1 of non-REM sleep (r = 0.345, p = 0.032), and b) stage 2 of non-REM sleep (r = 0.414, p = 0.009).

Therefore, SP appears to influence sleep characteristics, although further studies are required in order to define its role at nervous system.

P3061
Circadian rhythms of melatonin, cortisol and cytokines in pediatric obstructive sleep apnea syndrome

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Introduction: Several neuroimmunological mediators exhibit a circadian organization. Melatonin, cortisol and somnogenic cytokines can be altered in conditions of disturbed sleep.

Aims and objectives: The aim of the research is to investigate whether melatonin, cortisol, Tumor Necrosis Factor-α (TNF-α) and Interleukin-1β (IL-1β) show altered circadian rhythms in pediatric Obstructive Sleep Apnea (OSAS).

Methods: 47 children (26 OSAS, 21 not OSAS) underwent a nocturnal polysomnography and 2 blood samples were taken (2.00 am and 8.00 am). Cortisol and melatonin plasma concentrations were assayed using a radioimmunoassay technique. Cytokines were dosed from the supernatant of a 24-hours cell culture system (ELISA) in basal condition and after stimulation with phytohemagglutinin (PHA).

Results: The circadian organization of cortisol and melatonin was not altered in OSAS. In fact pediatric OSAS is not associated with an important sleep fragmentation that could affect circadian rhythms of hormones. Circadian rhythms of TNF-α and IL-1β had lost the nocturnal physiological peak and an additional early morning peak had developed (TNF-α: P<0.05). Cortisol and TNF-α basal levels were higher in OSAS than in controls (cortisol P<0.05 at 8.00 am). On the contrary TNF-α, after stimulation with PHA, was lower in OSAS than in controls (P<0.01 at h. 02.00 am and P<0.05 at h. 08.00 am). In addition we found higher melatonin levels in patients with an anamnestic agitated sleep.

Conclusions: The interaction among sleep regulation, circadian rhythms, inflammation, immunomodulation and hormone release is an interesting starting point for future research in this field.