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Childhood obstructive sleep apnoea and elevated blood pressure: A longitudinal follow-up study

Albert Li[1], Chun T. Au[1], Crover Ho[2], Yun K. Wing[2]. [1]*Department of Paediatrics, The Chinese University of Hong Kong, Shatin, Hong Kong;* [2]*Department of Psychiatry, The Chinese University of Hong Kong, Shatin, Hong Kong*

Background and objective: Childhood obstructive sleep apnoea (OSA) is a prevalent condition, and is associated with raised blood pressure (BP) in cross-sectional studies. This study aimed to investigate if baseline or changes in OSA severity could predict BP changes over a 4-year period.
Methods and results: Children who participated in our previous OSA prevalence study were invited to undergo repeat overnight sleep study and ambulatory 24-hr BP monitoring at 4-year follow-up. One hundred and ninety-one (62% out of 306) subjects took part in this follow-up study. Children with baseline moderate-to-severe OSA (OAHI >5/hr) had significantly higher BP at follow-up than controls. The change in OAHI was positively associated with the changes in wake and sleep systolic BP. Path analysis revealed a best-fit model in which log-transformed baseline OAHI and change in OAHI were both independent predictors for change in sleep systolic BP, after adjusting for baseline sleep systolic BP, gender, height and body mass index z score.
Conclusions: In the first longitudinal study that examined relationship between OSA and BP in children, we found baseline OSA severity could predict systolic BP at 4-year follow-up. The change in OAHI was associated with the change in sleep systolic BP, independent of obesity and weight gain. The results are clinically relevant since elevated BP in childhood is a well-known risk factor for future cardiovascular adverse events. Early diagnosis and intervention should thus be advocated in the management of childhood OSA.

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Adipokines in obese children and adolescents with sleep-disordered breathing

Kim Van Hoorenbeeck[1], Hilde Franckx[2], Patrick Debode[2], Luc Van Gaal[1], Kristine Desager[1], Wilfried De Backer[1], Stijn Verhulst[1]. [1]*Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Wilrijk, Belgium;* [2]*Obesity Program, Zeepreventorium, De Haan, Belgium*

Background: Sleep-disordered breathing (SDB) is prevalent in obesity. It has been linked to the metabolic syndrome. Possible mechanism is intermittent hypoxia of the fat tissue and alterations of adipokine secretion.
Aim: This study looked into the effects of intermittent hypoxia on adipokine levels before and after weight loss treatment.
Methods: Obese children and adolescents between 10-18 years were included while entering an inpatient weight loss treatment program. All patients had 2 visits: baseline and after 4-6 months of treatment. Leptin, adiponectin, TNF-alpha and IL-6 were determined at both visits and a sleep screening was performed at baseline and repeated in case of SDB.
Results: 158 patients participated in this study. Median age was 15.7 years (10.9-18.0). Mean BMI z-score was 2.75±0.42. 26% of participants had SDB at baseline. Mean nocturnal saturation correlated with leptin (r=0.19; P=0.02) and adiponectin (r=-0.17; P=0.04). IL-6 correlated with oxygen desaturation index (r=-0.20; P=0.02). TNF-alpha levels were not linked to sleep parameters. After weight loss 19% of subjects with SDB at baseline that participated in the follow-up study had residual SDB. Average weight loss was 29%. Correlation analysis did not show associations between improvements in sleep parameters and improvements in adipokines. These were mostly linked to a lowering in BMI z-score.
Conclusion: In an obese pediatric population SDB was linked to changes in the secretion profile of leptin, adiponectin and IL-6. After weight loss treatment levels of leptine, adiponectin, IL-6 and TNF-alpha did not improve in association with improvements in sleep parameters.

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Prevalence of obstructive sleep apnea syndrome in obese children (NANOS study)

María- Luz Alonso-Alvarez[1], Joaquín Terán-Santos[1], Cordero-Guevara José Aurelio[1], Ana Isabel Navazo-Egüia[1], Estrella Ordax-Carbajo[1], Monica Gonzalez-Martínez[3], Maria Jose Jurado-Luque[2], Odile Romero Santo-Tomas[2], María-Rosario Carpizo-Alfayate[3], Jaime Corral-Peñafiel[4], Juan Fernando Masa-Jimenez[4], Joaquin Duran-Cantolla[5], Cristina Martínez-Null[5], Antonia Barcelo-Bennassar[6]. [1]*Sleep Unit, CIBERES, Complejo Asistencial Universitario de Burgos, Burgos, Spain;* [2]*Sleep Unit, CIBERES, Hospital Vall D'Hebron, Barcelona, Spain;* [3]*Sleep Unit, Hospital Marques de Valdecilla, Santander, Spain;* [4]*Sleep Unit, CIBERES, Hospital San Pedro de Alcantara, Caceres, Spain;* [5]*Sleep Unit, CIBERES, Hospital Txagorritxu, Vitoria, Spain;* [6]*Sleep Unit, CIBER, Hospital Son Dureta, Palma de Mallorca, Spain*

Introduction: The most common cause of Obstructive Sleep Apnea Syndrome (OSAS) in children is the adenotonsillar hypertrophy. The prevalence of OSAS in obese children is unknown.
Methods: Aim: To determine the prevalence of OSAS in pediatric obese population.
Methods: Cross-sectional, prospective, multicenter study. The children included in the study came from general population of Spain, randomly selected, of both sexes between 3 and 14 years and body mass index (BMI) greater than or equal to percentile 95 for age and sex.
Medical history, snoring and Chervin questionnaires were performed in all children included, as well as, physical examination, nasopharyngoscopy, polysomnography (PSG) with Co2 recording and blood tests.
For the assessment of the sleep stages and respiratory events, the criteria of the AASM (2007), were used. The diagnosis of OSAS was made if the apnea hypopnea index per hour of sleep (AHI) was $\geq$ 3.
Results: 247 children were included: 135 males (54.7%), age from 4 to 14 with an mea age of 10.82 years (SD: 2.71). The mean BMI and the mean BMI Percentile were 28.01±4.72 and 96.82±0.59 respectively.
Of the 247 children studied, 122 of them (50.4%), reported the presence of snoring. The mean AHI was 5.60±9.91. 99 children were diagnosed with OSAS, so the prevalence of OSAS was 40.1% (95% CI 33.8% -46.4%).
The prevalence showed no statistically significant differences based on age or sex. The correlation between AHI and BMI was directly and significantly (r = 0.150, p = 0.018).
Conclusions: The prevalence of OSAS in obese children from general population is high 40.1%. Obesity in children suggests a possible risk factor for developing OSAS.
Funded: SEPAR and Mutua Madrileña.

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Results of a new questionnaire to assess sleep problems in childhood

Zsofia Lendvai, Gergely Kiss, Krisztina Pásti, Agnes Prókai, Attila J. Szabo. *Dept. of Pediatrics, Semmelweis University, Budapest, Hungary*

Screening of sleep disorders in children is of high importance. In Hungary there is no standardized questionnaire for assessing sleep problems.
We evaluated the results of sleep quality scales of our questionnaire and compared the data of healthy and clinical population. We analyzed the correlation between our questionnaire and validated tests and the severity of obstructive sleep apnea (OSA).
Our questionnaire is designed to estimate sleep hygiene and quality in two age groups (8-14 and 15-18 ys.) by nighttime and daytime symptoms score. Two groups of children were analyzed: 1. healthy group (n=2020), 2. children with sleep problems (n=66). The second group filled out two validated tests, Modified Pediatric Epworth Sleepiness Scale (MP-ESS), Conner's Rating Scales-Revised (CRS-R) and underwent polysomnography. Severity of OSAS was characterized by Apnea-Hypopnea Index (AHI) and Oxigen-Desaturation Index (ODI).
Children underwent polysomnography had significantly higher score both on nighttime and daytime symptoms scale than healthy children. Correlations were: score of nighttime symptoms scale and CRS-R score (r=0.441; p=0.001), score of daytime symptoms scale and MP-ESS score (r=0.389; p=0.001). Children in the highest quartile of nighttime symptoms scale had significantly higher AHI (mean±SD: 0.62±1.07 vs. 5.97±11.39; p=0,04) and ODI (mean±SD: 0.49±0,53 vs. 6.23±12,07; p=0.02) than children in the lowest quartile. The nighttime and daytime score index had higher sensitivity to predict OSA than other tests.
Our questionnaire can be potentially useful in evaluating sleep problems in children and give more information about sleep problems than other tests. However validation of the questionnaire is still needed.

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Long-term response of upper airway stimulation in obstructive sleep apnea

Wilfried De Backer[1], Johan Verbraecken[1], Lennart Knaack[2], Arie Oliven[3], Winfried Hohenhorst[4], Olivier Vanderveken[5], Paul Van de Heyning[5]. [1]*Dept of Pulmonary Medicine, Antwerp University Hospital, Antwerp, Belgium;* [2]*Zentrum für Schlafmedizin & Schlafforschung, Intersom, Köln, Germany;* [3]*Dept of Internal Medicine, Bnai Zion Medical Center, Technion, Israel;* [4]*Klinik für Hals-, Nasen- und Ohrenheilkunde, St. Anna-Klinik Wuppertal, Wuppertal, Germany;* [5]*Dept of ENT, Antwerp University Hospital, Antwerp, Germany*

Background: Previous studies identified patient selection criteria for therapy success in Upper Airway Stimulation (Inspire Medical Systems, USA) for treatment of moderate-to-severe OSA in patients intolerant to continuous positive airway pressure. The current study reported therapy response at 12-months post-implant in subjects who met selection criteria.
Methods: Among 34 implanted subjects, 18 met criteria for responder and 16 did not. AHI (Level 1 monitoring) were measured at 12 months. All patients were

monitored for device-related adverse events and patients met selection criteria were examined for therapy response during over-night PSG.
Results: There were no device malfunctions or un-anticipated device-related adverse events from 6-12 months. Among patients who met selection criteria and for which data are available, the AHI reduction was maintained at 12-month. Improvement for ESS and FOSQ were also observed in these subjects from baseline to 6-month, 10.7±5.4 to 7.5±4.1 (p=0.03), and 88.8±22.1 to 104.6±13.7 (p=0.01) for ESS and FOSQ, respectively. AHI remained unchanged at 12-month for patients that did not meet selection criteria.

AHI	Baseline	6-Mon	12-Mon
Responders (N=18)	33.9±6.2	17.0±18.5*	11.0±10.8*
Non-responders (N=16)	50.4±17.4	51.3±27.6	46.2±25.6

*Indicated significant changes from baseline (p<0.01).

Conclusion: The current study has demonstrated that Upper Airway Stimulation to treat OSA has a sustained therapy efficacy at 12-month post-implant in a selected group of moderate-to-severe OSA subjects.

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Targeted hypoglossal neurostimulation (THN) to treat obstructive sleep apnea (OSA). A one year safety and efficacy trial
Gimbada Mwenge[1], Philippe Rombaux[2], Myriam Dury[1], Benoit Lengele[3], Daniel Rodenstein[1]. *[1]Center for Sleep Medicine and Pneumology, Cliniques Universitaires Saint-Luc, Brussels, Belgium; [2]ENT, Cliniques Universitaires Saint-Luc, Brussels, Belgium; [3]Plastic Surgery, Cliniques Universitaires Saint-Luc, Brussels, Belgium*

Patients with severe OSA non-compliant to CPAP need an alternative treatment. We performed a one-year safety and efficacy study of a new therapy using unilateral THN. The system was implanted in 13 (12 males) out of 14 patients aged 50±10 yo, BMI 31±3 kg/m^2 with severe OSA refusing CPAP. After surgery two patients had asymptomatic hemitongue paresis lasting two and three months. One patient was not implanted due to a missmatch between the electrode and the pulse generator. There were no other surgery-related adverse events.
The main efficacy outcomes were the apnea-hypopnea index (AHI), the 4% oxygen desaturation index (ODI) and the movement arousal index (MAI). Diagnostic data showed AHI 45±18, ODI 29±20 and MAI 37±13. The Total Sleep Time (TST) was 414±85 min. After one year, AHI was 21±16, ODI 15±16, and MAI 25±14, all p<0.001, with unchanged TST (406±60 min). Nine patients reached AHI ≤ 20 and one patient an AHI of 22 at one year. Three patients were considered as failures: one patient had predominantly central apneas and an implanted morphine pump, one patient had an unusual long and thick uvula and the third one had no special features.
There were no serious adverse events. Three electrodes failures in two subjects led to treatment interruptions. One patient had his IPG replaced due to malfunction, and there was one twiddler phenomenon.
There was a trend towards improvements of the Epworth Sleepiness Scale (from 11±6 to 8±4, p 0.09) and of the Fatigue Severity Scale (5±2 to 4±2, p 0.09). Patients found the THN treatment more pleasant and comfortable than CPAP.
Conclusion: THN is safe and efficient in most OSA patients.

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Analysis of arousability of upper airway stimulation in obstructive sleep apnea
Johan Verbraecken[1], Joachim T Maurer[2], Lennart Knaack[3], Winfried Hohenhorst[4], Olivier Vanderveken[5], Paul Van de Heyning[5], Wilfried De Backer[1]. *[1]Dept. of Pulmonary Medicine, Antwerp University Hospital, Antwerp, Belgium; [2]HNO-Klinik, Universitaetsmedizin Mannheim, Germany; [3]Zentrum für Schlafmedizin & Schlafforschung, Intersom Köln, Köln, Germany; [4]Klinik für Hals-, Nasen- und Ohrenheilkunde, St. Anna-Klinik Wuppertal, Wuppertal, Germany; [5]Dept. of ENT, Antwerp University Hospital, Antwerp, Belgium*

Background: Previous studies showed that electrical stimulation of the hypoglossal nerve (N XII) can improve obstructive sleep apnea (OSA). In this study we looked to the effect on the different arousals indices in both responders and non-responders.

Polysomnographic results

	Baseline (pre implant)	6 Months after implantation
Responders (N=4)		
AHI (/h sleep)	32±15	11±7**
MAI (/h sleep)	34±12	9±3*
Total number of arousals	170±55	55±16*
Total number of respiratory arousals	64±31	8±8*
Non-Responders (N=3)		
AHI (/h sleep)	35±14	53±14
MAI (/h sleep)	34±6	38±13
Total number of arousals	200±51	201±81
Total number of respiratory arousals	102±53	125±95

*p<0.05, **AHI reduction of 50% and <20.

Methods: Upper Airway Stimulation (Inspire Medical Systems, Inc) systems were implanted in moderate-to-severe OSA patients who failed, or were intolerant of CPAP. The system is intended to reduce sleep apnea by stimulating the N XII to advance the tongue-base. AHI (events/hr), Micro Arousal Index (MAI, events/hr), total number of arousals and respiratory arousals were collected using lab-based PSG in 7 patients including comparison of responders (n=4) vs. non-responders (n=3) at baseline (pre-implant) and 6-M post-implant.
All arousal indices decreased statistically significantly in responders and there was no stimulation disturbance seen in the non-responder group.
Conclusion: Upper Airway Stimulation to treat OSA has a clear therapy efficacy at 6-M post-implant in a selected group of moderate-to-severe OSA subjects and that there is no arousal effect of the stimulation itself. It confirms the non-arousal effect of N XII stimulation as shown in our earlier pilot study (Arch Otolaryngol Head Neck Surg 2001;127:1216-23).

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Regional differences in characteristics of patients referred to European sleep centers. Results from the European Sleep Apnea Database (ESADA)
Tarja Saaresranta, Marisa Bonsignore, Ludger Grote, Jan Hedner, Walter McNicholas, Josep Montserrat, Thomas Penzel, Martin Pretl, Renata Riha, Pawel Sliwinski, Jan Zielinski. *Dept of Pulmonary Diseases, Turku University Hospital, Turku, Finland*

The ESADA contains multiple information from patients with suspected OSA at 22 European sleep centers. We analyzed regional differences in characteristics of 5,103 patients. Centers were grouped into the following regions: NORTH (Förde, NOR – Gothenburg, SWE – Turku, FIN), SOUTH (Barcelona, Cacéres, Lleida, ESP – Milan, Palermo, ITA – Haifa, ISR), EAST (Klaipeda, LTU – Kosice, SVK – Prague, CZE – Riga, LVA – Warsaw, POL), WEST (Dublin, IRL – Edinburgh, GBR) and CENTRAL (Antwerp, Brussels, BEL – Berlin, Giessen, GER – Paris, FRA).
Mean age was 51.8 (12.6) years in the cohort and females were slightly older than males. The highest and lowest prevalence of obesity (BMI>30) was found in the WEST and NORTH regions, respectively. The sleep study technique varied between regions, with the NORTH reporting more than 99% cardiorespiratory polygraphy compared with only 34% in the EAST. Sleep apnea severity varied between regions and the proportion of male patients with severe sleep apnea (AHI>30) was 23% in the NORTH compared with >40% in all other regions. Less than 50% of all patients reported severe daytime sleepiness (ESS>10); the highest ESS was found in patients in the WEST, the lowest scores in men in NORTH and women from EAST centers. Sleep length was 7.0 (1.8) hrs in women and 6.8 (1.6) hrs in men, and was shorter in the SOUTH compared with all other regions. No systematic regional differences were detected in frequency of comorbidities.
The data shows considerable regional differences between patients referred to European sleep centers, suggesting an influence of local referral patterns and/or phenotypic traits in Europe.