EFFECT OF WEIGHT CHANGE ON SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN CHILDHOOD OBESITY

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Abstract. In order to investigate the effect of weight change on polysomnographic (PSG) data in obese Thai children with obstructive sleep apnea (OSA), we recruited obese Thai children aged 1-15 years and performed PSG testing at baseline and then again after 1-2 years of outpatient weight loss therapy. Anthropometric and PSG data were compared between baseline and follow-up. A total of 35 children (17 boys, 18 girls), with a mean±SD age of 10.2±3.4 years were included. After a mean follow-up period of 19.7±4.5 months, there were 24 children who had lost weight and 11 children who had gained weight. The change in percentage weight for height (%W/H) significantly correlated with both change in apnea hypopnea index (AHI) (r=0.49; p<0.01) and change in mean oxygen saturation (SpO_2) (r=-0.44; p=0.01). Among obese children with weight loss at follow-up, statistically significant improvement was observed for apnea index (2.2 to 0.7; p<0.01), mean end tidal carbon dioxide ($P_{ET}CO_2$) (37.7 to 28.9; p=0.03), and maximum $P_{ET}CO_2$ (45.4 to 36.4; p=0.04). Increased apnea hypopnea index (AHI) during rapid eye movement (REM) sleep (5.3 to 16.4 events/hr; p=0.02) was found in the weight gain subgroup. In conclusion, weight change affects severity of OSA in obese Thai children with OSA. Weight loss was found to significantly improve apnea index and gas exchange in terms of carbon dioxide level, while weight gain caused worsening of AHI during the REM sleep stage. Further prospective study in a larger sample size, multi-center setting should be conducted.

Keywords: obstructive sleep apnea, childhood obesity, OSA

INTRODUCTION

Obesity is an evolving major public health concern. Prevalence of global childhood obesity increased from 4.2% in 1990 to 6.9% in 2010, with the rate predicted to be 9.1% by 2020 (Wang and Lobstein, 2006; de Onis *et al,* 2010). Obesity is an important cause of obstructive sleep apnea (OSA), which is defined as a disorder of breathing during sleep that is characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation and sleep patterns during sleep (Marcus *et al,* 2012). Degree of obesity was reported to be associated with OSA severity (Marcus *et al,* 1996; Wing *et al,* 2003; Xu *et al,* 2008; Udomittipong *et al,* 2011).

Prevalence of OSA has been reported to be much higher in obese children than in the general population (20-60% *vs* 1-4%, respectively) (Marcus *et al,* 1996; Wing *et al,* 2003; Lumeng and Chervin, 2008; Xu *et al,* 2008; Verhulst *et al,*

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2009). OSA can cause serious cardiovascular and neurocognitive consequences that result from sleep fragmentation and gas exchange abnormalities (O' Bien, 2014; Shamsuzzaman and Amin, 2014).

In 2012, the American Academy of Pediatrics (AAP) published an OSA guideline that recommends weight reduction in obese children, despite the fact that only a few studies have found and reported significant association between weight change and polysomnography (PSG) parameters (Marcus *et al,* 2012). As such, more studies are needed in different populations to establish a definitive relationship between body weight and OSA. Accordingly, the aim of this study was to investigate the effect of weight change on PSG data in obese Thai children with obstructive sleep apnea (OSA).

MATERIALS AND METHODS

This prospective cohort study was conducted in obese Thai children aged less than 15 years who were diagnosed as OSA by polysomnography (PSG) during the January 2010 to December 2011 study period at the Siriraj Sleep Center at Siriraj Hospital. Siriraj Hospital is Thailand's largest national tertiary referral center. The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (approval no. Si 486/2010). Written informed consent was obtained from the parent(s) or legal guardian(s) of each child, and assent was obtained from children aged >7 years prior to their inclusion in this study.

Obesity was defined as the percentage of ideal weight for height (%W/H) greater than 120, adjusted for age and gender. Degree of obesity was categorized as mild (%W/H of 120-139), moderate (%W/H 140-159), severe (%W/H 160-199), and morbid (%W/H ≥200). Severity of OSA is categorized by apnea hypopnea index (AHI) as mild (AHI of 1-4 events/hour), moderate (AHI of 5-10 events/hour), and severe (AHI >10 events/hour) (Katz and Macus, 2014).

All patients and caregivers were educated in the weight reduction plan every 3 months using an interdisciplinary approach that included pediatric endocrinologists and nutritionists. Patient's PSG, demographic, and anthropometric data were recorded at baseline and at a follow-up time point at least one year after the start of the weight reduction program. Any children with adenoid hypertrophy, tonsillar hypertrophy 3+ or 4+, neuromuscular disease, craniofacial anomalies, airway anomalies or chromosomal disorders were excluded.

Polysomnography (PSG)

Overnight PSG was performed using a Sandman Elite® version 8 computerized PSG system (Tyco, Ottawa, Canada). The following parameters were measured: electroencephalogram (F4-M1, C4-M1, O2-M1 and F3-M2, C3-M2, O1-M2); electrocardiogram; chin and leg electromyogram; left and right electrooculogram; airflow by oronasal thermistor and nasal pressure transducer; chest and abdominal effort using piezoelectric belts; body position; end-tidal carbon dioxide ($P_{ET}CO_2$) by Capnocheck® PLUS capnometer (SIMS BCI, Waukesha, WI); and, oxygen saturation using a Nellcor® pulse oximeter (Medtronic, Minneapolis, MN).

Children were continuously monitored by a pediatric sleep technician via an infrared video camera. Polysomnograms were manually scored by certified sleep technicians and interpreted by certified sleep medicine physicians. Sleep and associated events were scored using standard criteria from the American Academy of Sleep Medicine 2007 (AASM) (Iber *et al,* 2007).

Statistical analysis

Data analysis was performed using SPSS Statistics version 17 (SPSS, Chicago, IL). Paired Student's *t*-test or Wilcoxon signed-rank test was used to compare quantitative data, and chi-square test was used to compare qualitative

data between baseline and follow-up. Pearson correlation coefficient or Spearman's rank correlation coefficient was used to identify association between change in %W/H and PSG data. Data are expressed as number and percentage, mean ± standard deviation (SD), or median and interquartile range (IQL). A p-value < 0.05 was considered to be statistically significant.

RESULTS

Study group

Thirty-five obese Thai children (17 boys, 18 girls) with a mean±SD age of 10.2±3.4 years were enrolled. The mean time between baseline and the follow-up PSG evaluation was 19.7±4.5 months.

The mean baseline %W/H was 174.6±45.3%. Regarding classification of obesity, 7 cases were mild (20%), 11 cases were moderate (31.4%), 9 cases were severe (25.7%), and 8 children were morbidly obese (22.9%). At follow-up after the weight loss program, the overall mean %W/H decreased to 170.2±47.3%. At follow-up, 24 children had lost weight with a mean %W/H reduction of 7.2% from baseline. The remaining 11 children gained weight at the follow-up time point, with an in increase in mean %W/H of 9.2% (Table 1).

There were 17 cases with mild OSA (48.6%), 5 cases with moderate OSA (14.3%) and 13 cases with severe OSA (37.1%). At follow-up, 11.4% of children achieved normal PSG, 40.6% had severe OSA, and the rest had mild to moderate OSA (48.6%) (Table 1).

Relationship between change in %W/H and change in PSG

The change in %W/H (△%W/H) was found to be positively correlated with the change in AHI (△AHI) from PSG (r=0.49; p<0.01). In contrast, a negative correlation was observed between the change in mean SpO_2 (△mean SpO_2) and △%W/H (r=-0.44; p=0.01) (Table 2).

Table 1
Patient characteristics at baseline and at follow-up (N = 35).

Characteristics	Baseline	Follow-up
Age (yrs), mean±SD	10.2±3.4	11.8±3.5
% W/F, mean ±SD	174.6±45.3	170.2±47.3
Decrease (n=24)	179.4±51.8	166.4±53.3
Increase (n=11)	163.7±25.3	178.7±30.8
Degree of obesity, n (%)		
None (<120%)	0 (0.0)	1 (2.9)
Mild (120-139%)	7 (20.0)	10 (28.6)
Moderate (140-159%)	11 (31.4)	6 (17.1)
Severe (160-199%)	9 (25.7)	10 (28.6)
Morbid (>200%)	8 (22.9)	8 (22.9)
Severity of OSAS, n (%)		
Normal	0 (0.0)	4 (11.4)
Mild	17 (48.6)	9 (25.7)
Moderate	5 (14.3)	8 (22.9)
Severe	13 (37.1)	14 (40.6)

SD, standard deviation; W/H, weight for height.

Subgroup analysis of weight loss or weight gain on PSG

Of 24 cases in the %W/H reduction group, there was no significant change in AHI between baseline and follow-up. However, we found significant improvement from baseline to follow-up for the apnea index (2.2 to 0.7; $p<0.01$), mean $P_{ET}CO_2$ (37.7 to 28.9; $p= 0.03$), and maximum $P_{ET}CO_2$ (45.4 to 36.4 mmHg; $p=0.04$) (Table 3). In the increased %W/H subgroup, PSG data revealed a significant increase in AHI during rapid eye movement (REM) sleep from baseline to follow-up (5.3 to 16.4; $p=0.02$). Other parameters in the weight increase subgroup remained unchanged (Table 4).

DISCUSSION

In this study, change in %W/H had an effect on AHI and mean SpO_2 in children, regardless of degree of obesity. In subgroup analysis of the

Table 2
Correlation analysis between change in %W/H and change in polysomnographic (PSG) data.

Change after F/U of at least 1 year	%W/H	
	r	*p*
AHI (/hr)	0.49	<0.01*
Apnea index (/hr)	0.17	0.32
Hypopnea index (/hr)	0.34	0.05
Arousal index (/hr)	0.35	0.05
Desaturation index (/hr)	0.30	0.08
90-100% SpO_2 (%)	-0.08	0.64
Minimum SpO_2 (%)	0.05	0.79
Mean SpO_2 (%)	-0.44	0.01*
Mean $P_{ET}CO_2$ (mmHg)	0.05	0.87
Maximum $P_{ET}CO_2$ (mmHg)	-0.08	0.77

*$p<0.05$. W/H, weight for height; F/U, follow-up; AHI, apnea hypopnea index; SpO_2, oxygen saturation; $P_{ET}CO_2$, end tidal carbon dioxide.

Table 3
Polysomnographic (PSG) data of the decreased %W/H group (n=24).

Parameters	Mean±SD or median [IQR]		*p*-value
	Baseline	Follow-up	
Total sleep time (hr)	6.4±1.1	6.3±1.3	0.59
Sleep efficiency (%)	89.1±8.7	89.4±6.2	0.88
Sleep onset latency (min)	11.5±12.6	8.5±8.1	0.31
Stage of REM (% of TST)	15.3±7.1	14.4±5.8	0.63
Arousal index (events/hr)	9.8 [6.5-15.2]	12.4 [9.7-14]	0.70
Apnea index (events/hr)	2.2 [0.6-5.3]	0.7 [0.3-2.3]	<0.01*
AHI (events/hr)	7.4 [3.8-22.7]	8.9 [3.3-18]	0.35
NREM (/hr)	6.5 [2.5-18.3]	7.7 [2.7-14.6]	0.38
REM (/hr)	12.8 [5.9-44.7]	13.2 [4.4-39.1]	0.69
Mean SpO_2 (%)	97.2±1.3	96.9±1.7	0.51
Minimum SpO_2 (%)	85.9±4.9	86.3±5.6	0.79
Desaturation index (/hr)	3.2 [1.2-9.3]	3.2 [1.2-9.2]	0.91
Mean $P_{ET}CO_2$ (mmHg)	37.7±8.9	28.9±8.1	0.03*
Maximum $P_{ET}CO_2$ (mmHg)	45.4±9.4	36.4±7.1	0.04*

*$p<0.05$. W/H, weight for height; SD, standard deviation; IQR, interquartile range; REM, rapid eye movement; TST, total sleep time; AHI, apnea hypopnea index; NREM, non-rapid eye movement; SpO_2, oxygen saturation; $P_{ET}CO_2$, end tidal carbon dioxide.

weight reduction group, apnea index and both mean and maximum $P_{ET}CO_2$ were significantly decreased from baseline to follow-up. However, only AHI during the REM sleep stage was increased in the weight gain group.

Outpatient treatment seemed to have only modest effect on weight loss in our study (24 out of 35 cases), even though we formed an interdisciplinary team (endocrinology and nutrition specialists) to counsel and educate patients on diet and exercise strategies for weight reduction. There was no significant change in AHI in the weight reduction group between baseline and follow-up. Explanations include a reduction in %W/H (7.2%) that may have been too small to improve AHI and/or the fact that we had a study population of only 35 children. However, improvement in both apnea index and carbon dioxide (CO_2) was observed in the weight reduction group. These variables may be parts of the sleep architecture that improve earlier after obese children with OSA lose weight.

Verhulst *et al* (2009) studied teenagers who attended a residential treatment center for intensive weight loss for 4-6 months. With dietary restriction and a weekly physical training program, they found that a median weight loss of 24 kg (range: 11-48) or a body mass index (BMI) z-score reduction of 34.8% could decrease AHI from 3.8 to 1.9 events/hour (Verhulst *et al,* 2009). Another rehabilitation study reported that a mean BMI loss of 10.4 kg/m^2 resulted in a 50% decrease in respiratory disturbance index (RDI) (10.3 to 5.2 events/hour) (Siegfried *et al,* 1999). A study in patients who lost substantial amounts of weight reported that extensive weight loss

Table 4
Polysomnographic (PSG) data of the increased %W/H group (*n*=11).

Parameters	Mean±SD or median [IQR]		*p*-value
	Baseline	Follow-up	
Total sleep time (hr)	6.5±0.5	6.2±1.1	0.14
Sleep efficiency (%)	92.1±4.6	88.9±6.1	0.16
Sleep onset latency (min)	7.6±6.6	6.5±6.3	0.67
Stage of REM (% of TST)	18.2±13	14.9±5.0	0.29
Arousal index (events/hr)	6.8 [3.7-12]	12.4 [8.1-15.8]	0.05
Apnea Index (events/hr)	0.5 [0.4-2.9]	0.9 [0.2-1.7]	0.27
AHI (events/hr)	3.5 [2.6-6.3]	6.1 [4.7-13.3]	0.08
NREM (/hr)	3.2 [1.9-6.1]	5.3 [3.3-13.6]	0.27
REM (/hr)	5.3 [1.9-8.4]	16.4 [8.1-30.9]	0.02*
Mean SpO_2 (%)	97.7±1.1	96.0±1.9	0.05
Minimum SpO_2 (%)	85.9±6.7	82.1±8.9	0.29
Desaturation index (/hr)	1.9 [0.7-3.6]	4.6 [1.0-16.2]	0.07
Mean $P_{ET}CO_2$ (mmHg)	31.9±13.1	26.8±5.5	0.52
Maximum $P_{ET}CO_2$ (mmHg)	40.1±10.1	35.2±4.8	0.42

*p<0.05. W/H, weight for height; SD, standard deviation; IQR, interquartile range; REM, rapid eye movement; TST, total sleep time; AHI, apnea hypopnea index; NREM, non-rapid eye movement; SpO_2, oxygen saturation; $P_{ET}CO_2$, end tidal carbon dioxide.

(median 58 kg) as a result of bariatric surgery caused an almost 3-fold decrease in AHI (20.49 to 6.05 events/hour) (Kalra and Inge, 2006).

In contrast to the PSG benefits observed from weight loss, we found that a 9.2% increase in weight can lead to worsening of AHI during the REM stage from 6.5 to 22.8 events/hour. This highlights the importance of weight maintenance as a strategy for minimizing the progression of OSA severity. As observed from the modest improvements in %W/H in this study, more effective weight loss methods, such as intensive weight loss program or bariatric surgery, may be needed for patients to lose a sufficient amount of weight and to realize improvement in PSG parameters.

This study has some mentionable limitations. First, we decided to use %W/H instead of BMI, because a standard BMI curve is not yet available in Thailand. Second, the number of subjects in our study was small. Last, the patients included in our study were recruited from the sleep clinic of one hospital that is located in Bangkok – a large metropolis. It is, therefore, possible, that the findings of our study may not be generalizable to child and adolescent populations that reside in other parts of Thailand. Further multi-center study in a larger study population is needed to conclusively determine the effect of weight change on OSA and its complications in obese Thai children.

In summary, weight change affects severity of OSA in obese Thai children with OSA. Weight loss was found to significantly improve apnea index and gas exchange in terms of carbon dioxide level, while weight gain caused worsening of AHI during the REM sleep stage. Further prospective study in a larger sample size, multi-center setting should be conducted.

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CONFLICTS OF INTEREST

The authors hereby declare no personal or professional conflicts of interest regarding any aspect of this study.

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