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Original Article

Obstructive Sleep Apnea Effects on Pulmonary and Respiratory Muscle Function of Obese Children and Adolescents: A Preliminary Study

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Abstract

OBJECTIVE: Obstructive sleep apnea causes a marked decrease in lung volume and increases lung elasticity in obese adults. However, pulmonary and respiratory muscle function of obese children with obstructive sleep apnea who are more prone to develop airway obstruction than adults is less understood. This study aimed to determine the effects of obstructive sleep apnea on pulmonary and respiratory muscle function in obese children and adolescents compared to those without obstructive sleep apnea.

MATERIAL AND METHODS: This cross-sectional study enrolled 12 obese children and adolescents with a known polysomnographic diagnosis of obstructive sleep apnea and 12 controls that were matched for age, gender, and body mass index. Pulmonary function, maximal inspiratory pressure, maximum voluntary ventilation, and anthropometric variables were measured.

RESULTS Obese children and adolescents with obstructive sleep apnea exhibited significantly lower maximal mid-expiratory flow and displayed a forced expiratory flow at 50% and 75% of vital capacity (all $P < .05$) compared to the control group. However, there were no changes in other pulmonary function variables (all $P > .05$). Their maximal inspiratory pressure and maximum voluntary ventilation were lower than those of the controls, but this was not statistically significant (all $P > .05$).

CONCLUSION: Obstructive sleep apnea did not change pulmonary and respiratory muscle function in obese children and adolescents. The special assessment should be warranted to identify a reduction in maximal mid-expiratory flow and forced expiratory flow at 50% and 75% of vital capacity observed in this population.

KEYWORDS: Children, obesity, pulmonary function, respiratory muscle, sleep apnea
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INTRODUCTION

Obstructive sleep apnea (OSA), the most severe form of sleep-disordered breathing, is commonly found with a prevalence varying from 19% to 61% in obese children.[1] Obstructive sleep apnea in childhood is characterized by repetitive obstruction of the upper airway associated with hypoxia and arousals during sleep and/or increased respiratory effort secondary due to increased upper airway resistance and pharyngeal collapsibility, which subsequently induce sleep fragmentation, systemic alterations, and physical inactivity.[1,2] Studies showed that obstructed airways and hypoxia caused by OSA may overload pulmonary and respiratory muscle function.[3,4] A previous study reported that impaired inspiratory muscles were observed in adults with OSA.[5] Moreover, OSA could be worsened by obesity via mechanical stress upon the respiratory system affecting the diaphragm, lung volume, respiratory muscle function, work of breathing, and ventilator control.[6] A meta-analysis study[7] concluded that obesity causes deleterious effects on some pulmonary function variables including a decline in the ratio of forced expiratory volume in 1 second and forced vital capacity (FEV1/FVC), maximum mid-expiratory flow (MMEF), total lung capacity (TLC), and functional residual capacity (FRC) in children and adolescents. Reduction expressed as FEV1/FVC and the average FEF during the mid-portion of FVC at 50% and 75% of vital capacity (FEF_{25-75}) were more pronounced in children than adults. Additionally, it has been shown that obese adults with OSA, who have decreased lung volume, had a marked increase in the resistance of total respiratory and peripheral airways compared to those without OSA.[8] These results indicate that OSA combined with obesity might cause abnormally increased lung elasticity recoil pressure on exhalation which resulted in an increase in the severity of the airway obstruction. Furthermore, a diminished lung function which correlated with the severity of OSA was observed in obese children and adolescents.[3]

Thus, the aforementioned findings suggest that the coexistence of OSA and obesity may have more deleterious effects on respiratory function. However, it is unclear to what extent OSA combined with obesity has an impact on pulmonary and respiratory muscle function in children and adolescents who had more susceptible to airway obstruction than adults.[9] The understanding of how OSA combined with obesity affects the respiratory system in youth is important to clarify the nature of such disorders and to support clinical decision-making. Thus, the purpose of this study was to investigate the impacts of OSA on pulmonary and respiratory muscle function in obese children and adolescents compared to those without

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OSA. This study's hypothesis stated that obese children with OSA are more likely to be associated with impairments of pulmonary and respiratory muscle function than the controls without OSA.''

MATERIAL AND METHODS

Study Population and Sample Size Calculation

Based on the recommendation from Julious,[10] a flat rule of thumb was used and 12 participants per group would be needed for the pilot study. However, the stepped rule of thumb which requires 10 participants per group for estimating the variance to be used for the main trial sample size calculation provided a power of 90%, type I error rate of 5%, and a large (0.8) effect size.[11] Therefore, 12 obese children and adolescents aged 8-17 years underlying the polysomnographic (PSG) diagnosis of OSA and Sleep-Related Breathing Disorder-Pediatric Sleep Questionnaire (SRBD-PSQ) scores ≥0.33 were voluntarily enrolled. They were recruited at the Snoring Clinic at Chiang Mai University Hospital, Chiang Mai Province. The control group consisted of 12 obese children and adolescents from schools in Muang, Chiang Mai Province, who had SRBD-PSQ scores <0.33 that indicated non-OSA. Both groups were matched by age, sex, and body mass index (BMI). These participants were excluded in case of chest wall abnormalities, asthma, severe medical or mental illness, could not complete the pulmonary function test, or even those who had received any medical treatment that might affect the outcome variables.

Study Design

A cross-sectional study was conducted from February 2019 to January 2020. The protocol in this study was approved by the Ethics Committee of the Faculty of Associated Medical Sciences, Chiang Mai University (AMSEC-62ex-004), and written informed consent was obtained from the participants and their parents before data collection. Primary outcomes were pulmonary function testing, including FVC, FVC% predicted, FEV1, FEV1/FVC ratio, MMEF, $FEF_{25\%}$, $FEF_{50\%}$, and $FEF_{75\%}$, peak expiratory flow (PEF), maximal inspiratory pressure (PImax), and maximal ventilation voluntary (MVV). Secondary outcomes included anthropometric (body weight, stature, BMI, and skinfold thickness) variables. All outcomes were measured by well-trained assessors.

Diagnosis of OSA

Overnight polysomnograms were conducted in the hospital for monitoring PSG indices including the apnea–hypopnea index (AHI), ODI, and oxygen saturation (SaO_2) nadir by using a mobile sleep machine (SOMNOlab 2, Hamburg, Germany).[12] According to the criteria of Katz and Marcus,[13] OSA was defined if a participant had any of the following PSG index values: AHI ≥ 1 time/h or SaO_2nadir < 92%. The severity of OSA was classified based on either the AHI or SaO_2nadir (AHI < 1 or SaO_2nadir ≥ 92 = normal; 1 ≤ AHI < 5 or SaO_2nadir 86-91 = mild; 5 ≤ AHI < 10 or SaO_2nadir 76-85 = moderate; AHI ≥ 10 or SaO_2nadir ≤ 75 = severe).

SRBD-PSQ

The Thai version of 22-item SRBD subscale of PSQ was performed to assess the risk of OSA. The participant was considered to be at risk for OSA if PSQ scores ≥ 0.33.[14]

Experimental Protocol

All participants were seated and performed the anthropometric measurements, PImax, PFTs, and MVV, respectively, with a 5-minute intermission between the tests in the laboratory at a temperature of 25°C and a relative humidity of 56 ± 5%. All tests were completed at the same time of day, and verbal encouragement was provided during testing.

OUTCOME MEASUREMENTS

Anthropometric Variables

Body weight, stature, BMI, and skinfold thickness were determined using standardized techniques. Obesity was defined based on the International Obesity Task Force criteria.[15] Triceps and subscapular skinfold-thickness measurements were measured at the left side of the body using a Lange skinfold caliper (Beta Technology, Calif, USA) according to the standard method.[16]

Pulmonary Function Variables

Pulmonary function testing was conducted by using a computerized spirometer (Chestgraph HI-105; Chest MI Inc., Tokyo, Japan), according to the standardized procedure.[17] Each participant was instructed to sit and perform 2 to 3 trials for vital capacity practice followed by at least 3 acceptable FVC maneuvers. Pulmonary function testing includes FVC, FVC% predicted, FEV1, FEV1/FVC ratio, MMEF or $FEF_{25-75\%}$, $FEF_{25\%}$, $FEF_{50\%}$, $FEF_{75\%}$, and PEF were recorded. All values derived from spirometry are expressed as percentages of the predicted values for age and sex.

Maximum Inspiratory Pressure (PImax)

Maximum inspiratory pressure indicator of muscle strength was determined from residual volume (RV) and TLC with MicroRPM® (MICRO Medical®, Rochester Kent, UK) using standard procedures.[18] Participants were asked to perform a maximal inspiratory effort and hold it for 1 second. Three trials with a 1-minute interval between each were taken, and the highest value was chosen.

Maximal Ventilation Voluntary (MVV)

Maximal ventilation voluntary, which indicates the ventilatory mechanics and inspiratory muscle endurance,[19] was conducted according to the ATS/ERS guidelines[18] by using the Chestgraph HI-105 spirometer. Two trials of MVV maneuvers with a 5-minute interval was performed according to a previous study's guidelines.[20] Participants attached a nose clip and were instructed to breathe regularly in and out for 15 seconds with maximal voluntary effort.

Intra-rater Reliability of Data Collection

Each outcome measurements included anthropometry, PFTs and MVV, and PImax and was allocated to 3 raters, whereby the intra-rater reliability was performed. Five participants were chosen to administer each outcome for 2 trials with a 1-day interval between them. The intra-rater reliability of all variables was within an acceptable range (intraclass correlation coefficients (ICCs) > 0.9, all $P < .01$).

STATISTICAL ANALYSIS

The Shapiro–Wilk test was used to test for normality of data. It was found that all outcome variables were normally

distributed. Therefore, the mean and standard deviation (SD) were represented for continuous data. Count and percentage were represented for categorical data. Mean differences in PFTs, PImax, and MVV between the 2 groups were compared using an independent *t*-test. The ICC was calculated to assess the intra-rater reliability of the data collection. Significance was taken as $P < .05$ for all tests. All analyses were performed using the The Statistical Package for Social Sciences version 22.0 software (IBM Corp.; Armonk, NY, USA). Effect size was calculated from the pilot study results using G*Power software application (G*Power version 3.1.9.7 for Windows, Dsseldorf, Germany).

RESULTS

Study Participants

The characteristics of the study groups are given in Table 1. Fifty percent of children and adolescents with OSA had AHI ≥ 1 and all of them had SaO_2nadir < 92%. Based on the SaO_2nadir, the obese with OSA participants had 3 mild OSA (25%), 8 moderate OSA (66.7%), and 1 had severe PSG (8.3%). They were comparable to the obese without OSA group in age, gender, anthropometric variables but were significantly higher in SRBD scores ($P < .05$).

Pulmonary Function Variables

As shown in Table 2, the values of MMEF, $FEF_{50\%}$, and $FEF_{75\%}$ were significantly lower in the obese with OSA group compared to the obese without OSA group (all $P < .05$). No other differences in PFTs variables between the 2 groups were observed ($P > .05$).

Maximum Inspiratory Pressure (PImax) and Maximal Ventilation Voluntary (MVV)

An absolute value of PImax and MVV of the obese with OSA group were less than those of the controls, but this was not statistically significant ($P = .190$ and $P = .242$) (Table 3).

Table 1. Characteristics of the Obese Children and Adolescents With and Without OSA

Characteristics	Obese With OSA Group (n = 12)	Obese Without OSA Group (n = 12)	*P*
Age (years)	12.08 ± 2.43	12.00 ± 2.73	.938
Gender			
Female	2 (20%)	2 (20%)	n.a
Male	10 (80%)	10 (80%)	n.a
Anthropometric variables			
BW	80.68 ± 21.24	77.57 ± 19.20	.710
Stature	1.61 ± 0.14	1.58 ± 0.12	.653
BMI (kg/m^2)	30.62 ± 3.90	30.57 ± 5.18	.980
BSA	1.83 ± 0.32	1.78 ± 0.27	.685
Skinfold thickness (mm)			
Triceps	31.25 ± 5.91	35.17 ± 5.47	.106
Subscapular	37.00 ± 6.62	39.50 ± 9.13	.451
OSA definition by PSG indexes			
AHI (times/h)	2.07 ± 2.64	N/A	
ODI (times/h)	2.31 ± 1.68	N/A	
SaO_2 nadir (%)	83.17 ± 4.39	N/A	
SRBD score	0.51 ± 0.17	0.23 ± 0.04	.000*

Data are presented as mean ± standard deviation, unless otherwise.
*Significant differences between groups ($P < .05$).
AHI, apnea–hypopnea index; BMI, body mass index; BSA, body surface area; BW, body weight; ODI, oxygen desaturation index; OSA, obstructive sleep apnea; PSG, polysomnography; SaO_2nadir, oxygen saturation nadir; SRBD, sleep-related breathing disorder.

DISCUSSION

The results of the present study demonstrated that a significant reduction of MMEF, $FEF_{50\%}$, and $FEF_{75\%}$ were presented in the obese children and adolescents with OSA compared to their peers without OSA. Moreover, the other variables of pulmonary function, including FVC, FVC% predict, FEV1, FEV1/FVC, $FEF_{25\%}$, and PEF, and inspiratory muscle strength and endurance were not different between the 2 groups.

Pulmonary function tests using spirometry is useful for early screening of pulmonary defects.[21] In this study, we found that the values of FEV1/FVC ratio of obese children and adolescents with OSA and their peers without OSA were within the normal range. When compared to the normal-weight children and adolescents of the previous studies,[22,23] the values of FVC and FEV1 in our obese participants with OSA were lower but comparable to those in our obese participants without OSA. A concomitant decrease observed in both FVC and FEV1 and the normal FEV1/FVC ratio could possibly reflect premature closure of small airways in exhalation as mentioned earlier.[24] Additionally, our results found markedly decreased MMEF, $FEF_{50\%}$ and $FEF_{75\%}$ in the OSA group, except for $FEF_{25\%}$. A reduction of $FEF_{25\%-75\%}$ and decreased MMEF at low lung volume has been regarded as early changes in airflow limitation of small airways.[21] Also, there is empirical evidence that $FEF_{75\%}$ is a more sensitive parameter of small airway obstruction than FEV1 and FEV1/FVC ratio in children.[25,26] A study which determined lung volume and respiratory mechanical properties using a plethysmograph and an impulse oscillation system demonstrated that the OSA combined with obesity causes a decrease in lung compliance, which may in turn decrease FRC and increases airflow resistance in total respiratory and peripheral airways in adults.[8] In consistent with the study of Van Eyck et al[3] which found that all pulmonary function variables, especially FRC negatively, correlated with OSA severity.[3] Prior evidence and our findings showed a tendency of flow limitation in obese children and adolescents

Table 2. Pulmonary Function Variables

Pulmonary Function Variables	Obese With OSA Group (n = 12)	Obese Without OSA Group (n = 12)	*P*	Effect Size (*d*)
FVC (L)	2.92 ± 0.77	3.11 ± 0.70	.544	0.26
FVC predict (%)	92.87 ± 20.99	102.44 ± 17.24	.235	0.49
FEV1 (L)	2.48 ± 0.58	2.71 ± 0.59	.344	0.39
FEV1/FVC (%)	85.14 ± 5.57	89.65 ± 6.81	.090	0.72
MMEF (L/s)	2.69 ± 0.59	3.37 ± 0.81	.028*	0.94
$FEF_{25\%}$ (L/s)	4.20 ± 1.03	5.00 ± 1.57	.154	0.58
$FEF_{50\%}$ (L/s)	2.96 ± 0.72	3.71 ± 0.88	.031*	0.92
$FEF_{75\%}$ (L/s)	1.38 ± 0.31	2.00 ± 0.64	.006*	1.12
PEF (L/s*)	4.65 ± 1.11	5.20 ± 1.57	.329	0.39

Data are presented as mean ± standard deviation.
*Significant differences between groups ($P < .05$).
BMI, body mass index; BSA, body surface area; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FVC% predict, forced vital capacity percent predict; $FEF_{25\%}$, forced expiratory flow at 25% of the vital capacity; $FEF_{50\%}$, forced expiratory flow at 50% of the vital capacity; $FEF_{75\%}$, forced expiratory flow at 75% of the vital capacity; PEF, peak expiratory flow; MMEF, maximal mid-expiratory flow.

Table 3. The Absolute Values of Respiratory Muscle Function

Respiratory Muscle Function	Obese With OSA Group (n = 12)	Obese Without OSA Group (n = 12)	*P*	Effect Size (*d*)
PImax (cmH_2O)	2.55 ± 0.83	3.12 ± 1.18	.188	0.54
MVV (L/min)	78.42 ± 26.95	92.17 ± 29.00	.242	0.49

BMI, body mass index; BSA, body surface area; MVV, maximal voluntary ventilation; PImax, maximal inspiratory pressure.

with OSA; however, PFT used in this study is not the standard to evaluate small airway disease. Additionally, MMEF and flow toward the end of the forced expiratory maneuver have been reported that limit their sensitivity for detecting small airway disease in individual patients.[27,28] Therefore, further research is warranted before a clear conclusion can be drawn.

When analyzing the inspiratory muscle function, we also maintain that, although the inspiratory muscle strength and endurance in obese with OSA were lower than in those without OSA, no statistical difference was found. At the same age, the average PImax value of obese children with OSA in this study was similar to those of severe obese children that were tested in a previous study[29] and was inferior to those of normal-weight subjects.[30] Taken together, it is possible that the observed inspiratory muscle defect might be caused by the mechanical stress of obesity upon the respiratory system[6] as mentioned earlier, rather than OSA.

This study has some strength and limitations. To eliminate the confounding factors such as age, gender, and BMI, the protocol used in this study was performed by matches between OSA and non-OSA participants. Besides the limited availability and accessibility to PSG or even a mobile sleep machine, it's not a routine practice for children with obesity to use these tools for diagnosis of OSA. In this study, performing a portable sleep machine for participants with no OSA was felt to be impractical as did the OSA group. Instead, the SRBD-PSQ which have moderate accuracy for predicting OSA[14] was used to classify the OSA and non-OSA participants. As a result, false-positive or false-negative results for group classification could possibly happen and, in turn, affect the reliable of the main outcomes. Another limitation was the sensitivity of the portable sleeping tool which has been shown to be inferior to the standard PSG for diagnosis of OSA that might lead to underestimating or overestimating OSA severity.[31] Lastly, a cross-sectional study in small groups limits the ability to draw a causal relationship between pulmonary and respiratory muscle function in obese with OSA participants. Therefore, further studies using larger sample sizes and other parameters such as TLC, FRC, and RV are required to confirm our findings.

CONCLUSION

Obstructive sleep apnea did not modify pulmonary and respiratory muscle function in obese children and adolescents. Moreover, the observed reduction in MMEF and flow towards the end of the forced expiratory maneuver should be warranted using a standardized test.

Ethics Committee Approval: This study was approved by Ethics committee of the Faculty of Associated Medical Sciences, Chiang Mai University, (Approval No: XXXXXX).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.P., N.S., S.C.1, S.C.2, K.A., ; Design – S.P., S.C.1, S.C.2, K.A.; Supervision – S.P., N.S.; Resources – S.P., ; Materials – P.S., K.W.; Data Collection and/or Processing –N.S., S.C.1, S.C.2, K.A., P.S., , K.W.; Analysis and/or Interpretation – S.P., N.S., S.C.1, S.C.2, K.A., P.S., K.W.; Literature Search – S.P., S.C.1, S.C.2, K.A., P.S., K.W., ; Writing Manuscript – S.P., S.C.1, S.C.2, K.A., P.S., K.W.; Critical Review – S.P., N.S., S.C.1, S.C.2, K.A.

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