The effect of childhood obesity on respiratory function tests and airway hyperresponsiveness

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The aims of this study were to investigate the effect of exogenous obesity on respiratory function tests, to define the relationship between the severity of obesity and respiratory function test parameters, and to detect the incidence of airway hyperresponsiveness and exercise-induced bronchospasm in an obese study group.

This cross-sectional controlled study was done with 38 exogenous obese patients, aged 9 to 15 years, and 30 healthy children. Basal respiratory function test parameters were measured with spirometry. To display airway hyperresponsiveness, 4.5% hypertonic saline provocation test was used; exercise-induced bronchospasm incidence was defined with bicycle ergometry.

Basal respiratory function test parameters were lower in the study group as compared with the control group. Exercise test was positive in 31.6% of the obese group and in 3.3% of the control group (P=0.003). The provocation test with hypertonic saline test was positive in 18.4% of the obese group. There were strong negative correlations between body mass index (BMI), relative weight, skin fold thickness, waist/hip circumference ratio and basal forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and peak expiratory flow (PEF) values. The diagnosis and management of exercise-induced bronchospasm may improve exercise performance and physical activity, assist with weight loss, and break the vicious circle.

***Key words:** exogenous obesity, respiratory function tests, exercise-induced bronchospasm, airway hyperresponsiveness, asthma, childhood.*

Obesity is a multifactorial disease leading to social, psychological and medical problems[1]. In 1998 the World Health Organization (WHO) designated obesity as a global epidemic[2]. Obesity negatively affects the respiratory and other systems in many ways, and previous studies have demonstrated an association between obesity and pulmonary dysfunction. Obesity has a direct effect on the mechanical behavior of the respiratory system by altering lung volume, airway caliber or respiratory muscle strength[3-5].

Most of the studies evaluating the relationship between obesity and respiratory function tests were done in adults; investigations about this subject in childhood are limited.

The aims of this study were to extend the findings of previous studies by explaining the effect of obesity on respiratory function tests in childhood, to define the relationship between the severity of obesity and respiratory function test parameters, and to detect the frequency of exercise-induced bronchospasm and airway hyperresponsiveness in the study group.

Material and Methods

This cross-sectional controlled study was done between 2001 and 2002. Thirty-eight patients aged 9 to 15 years, recently diagnosed as exogenous obesity in Ege University Pediatric Outpatient Clinics, and 30 healthy children in the same age group as controls were recruited for the study. All the subjects were symptom-free and had no clinical evidence of cardiopulmonary disease in a preceding evaluation.

Inclusion criteria for the study were as follows:

- Age between 9 to 15 years old.
- Diagnosis of exogenous obesity based on clinical and laboratory findings.
- Body mass index (BMI) more than 85th percentile or more than 25 kg/m^2[2]. Exclusion criteria for the study were as follows:
- Diagnosis of endogenous obesity.
- Presence of any sign of cardiorespiratory system disease.
- Medical history of atopy and active cigarette smoking.
- Presence of medical conditions in which exercise was forbidden.

Informed consents were obtained from the families of all patients.

Information regarding demographic properties, passive cigarette smoking, family history of atopy, performance of regular sportive activity, duration of being fed with mother's milk, and past medical history of lung infection was collected from the study and control groups via face-to-face questionnaire performed by the same investigator.

Measurements of weight, height, waist and hip circumference, thickness of the triceps and subscapular skinfolds, relative weight and BMI were done using standardized methods.

Weight was measured in kilogram with Tefal electronic device with 100 g intervals. Height was measured with 0.1 mm intervals by Ravel Harpenden Stadiometer in centimeter (cm). Waist and hip circumferences were measured at the narrowest area above the anterior iliac spine and widest area above the hip, respectively, in cm. Measurements of triceps and subscapular skin fold were done with Holtain caliper (0.1 mm intervals) at the midpoint of acromion-olecranon of extended left arm and just below the left scapula vertically. Logarithmic conversion of subscapular and triceps skin fold thickness was done according to age and sex.

The relative weight was the ratio of the patient's weight to ideal weight according to height. Relative weight more than 120% and BMI (weight/height^2) more than 95th percentile according to age and sex were accepted as obesity.

To evaluate fat distribution, waist and hip circumferences were measured and the ratio of waist circumference to hip circumference was calculated for each patient.

Spirometric Measurements

Respiratory function parameters were measured with ZAN®messgeraete GmbH spirometry in accordance with recommendations of the European Respiratory Society at room temperature by the same investigator. Before each measurement spirometry was calibrated. Subjects were rested for 15 mins before measurements and informed about the procedure. After appropriate placement of mouthpiece and nose click, powerful, quick, forced expiration challenge was done just after maximum forced inhalation. While doing this maneuver, flow and volume curves were followed on the screen to detect whether or not subjects displayed enough effort during inspiration and expiration. By doing at least three technically appropriate measurements, the highest value was recorded as basal value. Forced vital capacity (FVC) (L), forced expiratory volume in one second (FEV1) (L), FEV1/FVC (%), peak expiratory flow (PEF) (L/s), and forced expiratory flow between 25% and 75% of vital capacity (FEF25-75) (L/s) were measured with spirometry. All these parameters were represented as percent of Polgar reference values, which were designated according to age, sex, weight and height[6].

Exercise Test

Subjects with FEV1/FVC ratio of >70% were accepted for this test. All the patients fulfilled this criterion. Monak Bicycle Ergometry with adjustable sitting height and load of work was used in this test, and during the test, heart rate was monitored with Polar heart rate device. The work load level was increased gradually till the heart rate increased 90% of maximum value for age and respiratory rate reached 70% of maximum value for age. After attaining sufficient increment in the heart and respiratory rate, 8 mins of exercise were done. FEV1, FVC, FEV1/FVC ratio were measured at the 0.5, 10, 15, 20, 25, and 30th mins, and differences from the basal values were recorded. Exercise test was accepted as positive if the FEV1 decreased 10% or more from the basal level[7].

Hypertonic Saline Provocation Test

All the patients underwent this test. If the exercise test was positive, provocation test was done after FEV1 reached basal level. To detect airway hyperresponsiveness, hyperosmolar 4.5% NaCl was inhaled with ultrasonic Master nebulizer. Duration of inhalation was increased gradually (0.5, 1, 2, 4 and 8th mins). Inhalations were applied at three-minute intervals and spirometric measurements were undertaken 1 min after inhalations. Provocation test was accepted as positive if the FEV1 decreased 15% below the basal level, and the test was ended. If the decrease in FEV1 was between 10 to 15%, the same inhalation duration was repeated. If the decrease was again 10-15%, inhalation duration was doubled. Hypertonic inhalation test was accepted as negative if at the end of 15.5 mins of inhalation, decrease in FEV1 was not more than 15%[8].

Reversibility Test

This test was applied to subjects whose exercise and/or provocation tests were positive. Terbutaline sulfate was used for the test and it was inhaled twice with an interval of less than three seconds, and FEV1 was measured 15 mins later. If the difference in FEV1 measurements before and after inhalation was more than 12%, the test was accepted as positive.

Statistics

Student's t test was used for comparison of variable averages. Pearson chi-square and Fisher's exact chi-square tests were used to compare the frequency distribution of grouped variables. Relationship between two variables was represented with correlation coefficient. P value less than 0.05 was accepted as statistically significant. For the database and statistical analysis, SPSS 10.00 pocket program was used.

Results

Thirty-eight exogenous obese subjects between the ages of 9 to 15 years (average age: 11.71±1.79 years) were accepted for the study and 30 healthy children in the same age group (average age: 11.66±1.95 years) constituted the control group. Male/female ratios of the obese and control groups were 22/16 and 16/14, respectively. All the demographic properties of the study and control groups were similar except for family history of obesity, which was more common in the study group (92% and 33.3%, respectively).

Demographic properties of the study and control groups are shown in Table I.

The average values of weight, height, BMI and relative weight of study group were higher than of the control group, and the differences was statistically significant (Table II).

The average values of the waist and hip circumference, skin fold thickness and the ratio of waist to hip circumference were higher in the study group (Table III).

Average of basal FVC, FEV1, PEF and FEF25-75 measurements, represented as percent of expected values, were lower in the study group as compared with the control group, and this was statistically significant. However, the averages of FEV1/FVC ratio of the two groups were similar (Table IV).

Exercise test was positive in 31.6% (12 patients) of the obese group and 3.3% of the control group, and this difference was statistically significant (P=0.003). In the obese group, most

Table I. Demographic Properties of the Obese and Control Groups

	Obese N=38	Control N=30	P value
Age (year)	11.71±1.79	11.66±1.95	P=0.781
Sex (M/F)	22/16	16/14	P=0.707
Passive cigarette smoking (%)	49.9	46.6	P=0.263
Performing regular sportive activity (%)	13.3	21.1	P=0.528
Exposure to pet (%)	5.2	3.3	P=0.415
Family history of atopy (%)	0	6.7	P=0.106
History of lung infection (%)	6.7	2.6	P=0.421
Family history of obesity (%)	92	33	P=0.000*

* Statistically significant.

Table II. Average Weight, Height, BMI, and RW of the Obese and Control Groups

	OBESE GROUP (N= 38)	CONTROL GROUP (N=30)	P value
Weight (kg)	66.33±13.86 (41.20–96.70)	42.55±11.58 (25.8–65.5)	P<0.001*
Height (cm)	154.41±11.63 (132.5–181)	148.80±15.08 (124.5–178)	P=0.88
BMI (kg/m²)	28.18±2.67 (25.12–32.70)	18.80±1.97 (15.03–22.05)	P<0.001*
RW (%)	138±10.99 (121–159)	98±8.19 (87–118)	P<0.001*

* Statistically significant. BMI: Body mass index. RW: Relative weight.

Table III. Waist–Hip Circumferences, Waist/Hip Circumference Ratio, and Skin Fold Thickness of the Obese and Control Groups

	Obese group (N=38)	Control group (N=30)	P value
Waist circumference (cm)	87.02±7.04 (72–101)	63.5±7.06 (54–84)	P<0.001*
Hip circumference (cm)	99.03±8.33 (83–117.50)	79.11±9.77 (62–95)	P<0.001*
Waist/Hip Circumference Ratio	0.87 (0.81–0.97)	0.80 (0.67–0.95)	P<0.001*
Triceps Skin Fold Thickness (mm)	29.60±6.3 (12–38.4)	12.4±3.5 (7–22)	P<0.001*
Subscapular Skin Fold Thickness (mm)	27.63±7.01 (10-39)	10.03±4.7 (4.5-17)	P<0.001*

* Statistically significant.

Table IV. Basal Respiratory Function Test Parameters of the Obese and Control Groups

	Obese (N=38)	Control (N=30)	P value
FVC (L) (% of expected value)	2.70±0.63 (85±7.0)	2.95±0.8 (107±10)	P<0.001*
FEV1 (L) (% of expected value)	2.43±0.61 (90±7.5)	2.59±0.77 (109±11.1)	P<0.001*
PEF (L/s) (% of expected value)	4.53±1.05 79.5±16.4	5.35±1.30 105±8.0	P<0.001*
FEF25-75 (L/s) (% of expected value)	2.85±0.65 90±9.2	3.16±0.85 103±7.6	P<0.001*
FEV1/FVC (%)	92.52±6.95	94.52±6.95	Not significant

* Statistically significant. FVC: Forced vital capacity. FEV1: Forced expiratory volume in 1 second. PEF: Peak expiratory flow. FEF25-75: Forced expiratory flow between 25%-75% of vital capacity.

of the positive exercise tests were detected at the 0 and 5th mins, respectively. Average age of these 12 patients was 11.90±1.64 years. Out of 12 obese patients with positive exercise tests, seven were female.

The provocation test with hypertonic saline was positive in 18.4% (7 patients) of the obese group, whereas in the control group there was no positive test result (Table V), and this difference was also statistically significant. Average age of obese patients with positive hypertonic saline tests was 12.14 ±1.95 years, and five of the seven patients were female. In all of the patients with positive hypertonic saline provocation test, exercise tests were also positive. Positive test results were obtained in three subjects after 2 mins, in two subjects after 4 mins, and in one subject after 1 min of hypertonic saline inhalation.

were also positive. There were strong negative correlations between BMI, relative height, skin fold thickness, waist/hip circumference ratio and basal FVC, FEV1 and PEF values (Table VI).

Discussion

The prevalence of childhood obesity is increasing throughout the world[1,3,4-5]. Many studies have demonstrated an association between obesity and pulmonary dysfunction.

In this cross-sectional controlled study, we studied the effect of childhood obesity on basal respiratory function tests and the relation between the severity of obesity and respiratory function test parameters, and we determined the incidence of exercise-induced bronchospasm and airway hyperresponsiveness among obese children. Thirty-eight exogenous obese subjects

Table V. Exercise and Hypertonic Saline Provocation Test Results of Obese and Control Groups

	Obese N=38	Control N=30	Statistics
Exercise test (%)			
(+)	12 (31.6%)	1 (3.3%)	Chi^2= 8.65
(–)	26 (68.4%)	29 (96.7%)	p=0.003*
Hypertonic saline provocation test (%)			
(+)	7 (18.4%)	(–)	Chi^2= 6.16
(–)	31 (81.6%)	30 (100%)	p=0.013*

* Pearson chi-square test.

Table VI. Correlation Coefficients Between the Body Measurements and Respiratory Function Test Parameters

	FEV1 (L/s)	FVC (L)	PEF (L/s)	FEF25-75 (L/s)
BMI (kg/m²)	-0.65*	-0.71*	-0.69*	-0.51
RW (%)	-0.64*	-0.70*	-0.66*	-0.46
Subscapular skinfold thickness (log)	-0.62*	-0.65*	-0.70*	-0.37
Waist/Hip ratio	-0.28*	-0.41*	-0.43*	-0.23
Triceps skinfold thickness (log)	-0.62*	-0.65*	-0.69*	-0.23

* Correlation coefficient, Pearson correlation test, p<0.001
Underlines indicate strong relationship.
FEV1: Forced expiratory volume in 1 second. FVC: Forced vital capacity. PEF: Peak expiratory flow. FEF25-75: Forced expiratory flow between 25%-75% of vital capacity. BMI: Body mass index. RW: Relative weight.

There was no concomitant fall in FVC in the obese patients with positive exercise and/or hypertonic saline provocation test. The change in FEV1/FVC ratio was similar to that of FEV1 in these patients. In all of the subjects with positive exercise and/or hypertonic saline provocation test, reversibility tests

were enrolled in the study, and 30 healthy children in the same age group constituted the control group.

In this study, basal values of FVC, FEV1, PEF and FEF25-75 in the obese group were lower in comparison with the control group. Since these parameters are affected by weight, height, age and sex, reference values were used[6], and measurements of these parameters were represented as percent of reference values. Unfortunately, there is no available respiratory function test parameter reference for Turkish children, so Polgar's reference values were used.

The findings of baseline lung function were similar to those of previous studies by other groups that performed only spirometry[9,10]. Most recent studies have reported reduction of lung volumes and diffusion capacity of carbon monoxide to be the most prevalent lung function parameter alterations in obese children[11]. Unfortunately, lung volumes were not measured in this study, but the baseline parallel alterations in FEV1 and FVC were compatible with a reduction in functional residual capacity (FRC) with increasing BMI. This shift in FRC will increase respiratory resistance as shown in adults with obesity[5].

In a study of Lazarus et al.[12], adjusted FVC and FEV1 values in children decreased significantly with increasing total body fat percent. Within each age and gender group, ventilatory function decreased with increasing proportion of body fat. Similar to this result, in our study, there were strong negative correlations between FVC, FEV1 and skin fold thickness. In an adult study, it was reported that body fat distribution has independent effect on lung function[13,14]. However, in our study it was seen that decrease in FEV1 and FVC was more strongly correlated with excess subcutaneous fat rather than fat distribution as determined by waist to hip ratio.

The question of how obesity affects pulmonary function tests has been explored in a number of studies.

Inselma et al.[9] claimed that obese children have altered pulmonary function, which is characterized by reductions in lung diffusion capacity, ventilatory muscle endurance and airway narrowing. These alterations may reflect extrinsic mechanical compression on the lung and thorax, and/or intrinsic changes within the lung. The reduced diffusion capacity may result from decrease in alveolar surface area relative to lung volume.

In a study done by Zerah et al.[5], expiratory flows diminished in proportion to lung volumes, and the FEV1/FVC ratio was within normal limits in obese patients. In our study, FEV1/FVC ratios of the study and control groups were also similar. This means both respiratory resistance and airway resistance rise significantly with the level of obesity. These findings suggest that in addition to the elastic load, obese subjects have to overcome increased respiratory resistance resulting from the reduction in lung volumes related to being overweight.

In another study, it was shown that after weight loss, significant increases were detected in FRC, residual volume, total lung capacity, and expiratory reserve volume[15]. Unfortunately, we could not provide enough weight loss in our study group to repeat respiratory function test parameters.

In the past two decades there has been a significant increase in the prevalence of both asthma and obesity worldwide[16,17]. Previous cross-sectional studies have shown an association between obesity and asthma[18-20]. However, the nature of the relationship has not been established and, furthermore, if the association is causal, the direction of causation remains unknown.

In this study, although there was no asthma symptoms, airway hyperresponsiveness was positive in 18.4% of the obese subjects, and this was statistically higher than in the control group.

We used hypertonic saline for the provocation test in our study. In the literature, this provocation test was found to be effective and reliable for detection of asthma in children[8,21,22]. Exercise-induced asthma has a closer relationship to bronchial responsiveness to hypertonic saline aerosol than to non-specific reactivity demonstrated by histamine challenge[21].

Since patient cooperation is less necessary in hypertonic saline provocation test, it is easy to apply in children, and test positivity usually can be determined very early. Low cost is the other important advantage of this test. Hypertonic saline test positivity incidence in the study group was 18.4%, and this was statistically significant. In an adult study, airway hyperresponsiveness tested with histamine was not found to be increased in obese patients although they reported more wheezing and shortness of breath. In our study, all the patients with positive test results were symptom-free. In the literature, exercise test positivity incidence in healthy populations is reported as less than 5%. In our control group test positivity was 3.3%. Positive exercise test supports the diagnosis of asthma, but negative test can not exclude the asthma[23]. In our study, exercise test was positive in 31.6% of obese patients and this was statistically significant when compared with the control group. These patients previously had no symptom, indicating the exercise- induced asthma. During epidemiologic surveys using exercise, investigators have been surprised by the number of positive test results in children who do not report symptoms and do not have positive responses to histamine[24]. There are many possible reasons for this. Breathlessness often accompanies vigorous exercise in children. Exercise-induced asthma usually is brought on after exercise, at least in mild to moderate cases, and breathlessness following exercise may be simply thought of as a normal response to exercise. In addition, refractoriness to exercise occurs in 50% of asthmatic children, so exercise-induced bronchospasm may be intermittent and not perceived by the child as a respiratory problem related to exercise. Further, a diagnosis of exercise-induced asthma is made when the decrease in PEF or FEV1 is greater than 10% or 15%, yet few children complain of symptoms of asthma until the FEV1 has fallen by 25% or more. Similarly, wheeze may not be audible until the FEV1 has fallen by 30%. In one study, the spirometric response to the exercise challenge in asthmatic and non-asthmatic obese children was investigated and it was concluded that the non-asthmatic obese children had a significant decrease in FEV1 compared to the asthmatic non-obese children[25]. In a study of Kaplan et al.[10], the frequency, degree, and the pattern of bronchial reactivity to exercise were compared in 13 obese and 14 control children, ages 6 to 10 years, with no history of asthma, and it was demonstrated that significantly greater frequency and degree of bronchospasm occur in obese children. It can be claimed that the FEV1 following the exercise test may be reduced to a greater extent because the FVC was reduced due to fatigue or poor fitness in the obese group. But there was no change in FVC following exercise provocation, thus, change in FVC following exercise is not a feasible explanation for the reduction in flow rates.

In conclusion, in this study, basal respiratory function test parameters were found to be lower in the obese group. In addition, airway hyperresponsiveness and exercise-induced bronchospasm frequencies were high in the obese subjects. Whether exercise-induced bronchospasm leads to exercise avoidance and obesity or whether obesity causes or enhances bronchial hyperreactivity to exercise requires further study. The diagnosis and management of exercise-induced bronchospasm may improve exercise performance and physical activity, and assist in weight loss, thereby breaking the vicious cycle. A routine respiratory function test can be recommended to obese patients, especially the ones with physical inactivity, for early diagnosis of exercise-induced bronchospasm.

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