Pulmonary and extrapulmonary features in bronchopulmonary dysplasia: a comparison with healthy children

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Abstract. [Purpose] The aim of this study was to compare functional capacity and peripheral muscle strength in preterm children with bronchopulmonary dysplasia (BPD) with those of age-matched full-term healthy controls. [Subjects and Methods] Eighteen BPD subjects and 20 healthy subjects were enrolled in the study. Pulmonary function testing was performed. Body composition was determined using the skinfold method. An analysis of posture was scored. Muscle strength was evaluated using a dynamometer. Functional capacity was assessed using the six-minute walking test (6MWT). [Results] Pulmonary function testing parameters, 6MWT distance, and quadriceps strength of the children with BPD were significantly lower than those of healthy peers. The scores of posture analysis of the children with BPD were significantly higher than those of healthy subjects. Exercise heart rate was significantly higher in the children with BPD compared to healthy children. The 6MWT distance correlated with height, fat-free mass, exercise dyspnea perception, and hand grip strength in BPD children. [Conclusion] The study showed that preterm children with BPD had disturbed pulmonary and extrapulmonary characteristics. BPD had lower fat free mass, reduced lung function, worsen postural function, a shorter 6MWT distance, and lower quadriceps strength than healthy children. These features may provide insights into the choice of outcome measures for pulmonary rehabilitation for BPD.

Key words: Bronchopulmonary dysplasia, Functional capacity, Lung function

INTRODUCTION

Bronchopulmonary dysplasia (BPD) is a chronic lung disease affecting premature infants1). BPD begins in the neonatal period but its effects can continue long term, through to adulthood. Premature infants with BPD have an increased rate of hospitalization for respiratory illness and need for respiratory medications, compared to those without BPD3).

Adverse respiratory outcomes are one of the important long-term morbidities in survivors following premature birth. Lung function of preterm children is lower than normal, and those who also suffer from BPD have an even greater reduction in lung function. They have reduced forced expiratory flows (lower forced expiratory volume in one second [FEV1]) with normal forced vital capacity (FVC) and total lung capacity (TLC); higher residual volume (RV) and RV/TLC ratio; and show airway obstruction and air trapping as compared to healthy infants born at term3). Functional residual capacity and ventilation inequality are independently associated with the use of supplemental oxygen4, 5). Intermittent positive pressure ventilation, prolonged oxygen therapy, and maternal smoking are the main risk factors of reduced lung function in childhood period of BPD6).

Respiratory problems can lead to a reduction in the functional exercise capacity of children with BPD who were born prematurely. Studies have shown that children born prematurely have functional capacity impairment with expiratory flow limitation and increased oxygen consumption during exercise, compared with children born at full term3). However, some studies with small sample sizes demonstrated that maximal cardiopulmonary exercise testing parameters were similar in preterm children with and without BPD7, 8). The discrepancy in the findings may be explained by the use of different exercise testing protocols. Children and adolescents with BPD participate in daily physical activities without symptoms8). Children with BPD at preterm frequency present delayed growth and undernutrition9–11). Vogt et al. suggested that preterm children may have muscular
deconditioning due to their significantly reduced workload compared to healthy subjects\(^2\).

Pathological changes in the neonatal period contribute to reduced lung function through the use of oxygen supplementation and the duration of mechanical ventilation. Whether, BPD with preterm birth is also associated with diminished functional exercise capacity and muscle strength later in life is not yet known. The aim of this study was to compare pulmonary and extrapulmonary features (functional capacity and peripheral muscle strength) of children with BPD with those of age-matched full-term controls.

Subjects and Methods

This cross-sectional study was conducted with two groups of children aged 6–13 years. The group of BPD children comprised children with gestational ages of less than 32 weeks and/or a birth weight under 1,500 g. Bronchopulmonary dysplasia was identified by the need for oxygen supplementation for at least 28 days and chronic changes on chest radiography\(^1\). All patients received a standard medical treatment in the postnatal period. The BPD children with neurologic disorders like cerebral palsy and cognitive deficits (n=5) were excluded due to the difficulty of performing exercise tests and muscle strength measurements with such subjects. Therefore, 18 subjects with BPD (10 females, 8 males) were enrolled. The control group comprised 20 healthy subjects (12 females, 8 males) who were born at full-term after more than 37 weeks of gestation, and had no medical history of cardiac, pulmonary or muscular disorders, and were volunteers from among the relatives of researchers and staff. The protocol was approved by the Committee for Ethics in Research of the Hacettepe University. Written informed consent was received from all the children and their parents.

Physical and demographic characteristics of the subjects were recorded. Data from the postnatal period regarding the use of mechanical ventilation or non-invasive ventilation, such as nasal continuous positive airway pressure and supplemental oxygen were recorded.

Body mass index (BMI) was calculated by the formula of weight/height\(^2\) (kg/m\(^2\)). Fat free mass (FFM), fat mass (FM), and percentage of body fat were determined using the skinfold thickness method from four (biceps, triceps, subscapular, and suprailliac) different regions using a skinfold caliper (Skinfold Caliper, Holtain Ltd., Crosswell, UK). Measurements were repeated three times on the dominant side and the mean of the three measurements was used\(^1\)

Pulmonary function testing was performed using a spirometer (SensorMedics, 6200 Body Box, Viasys, USA). The FVC, FEV\(_1\), FEV\(_1\)/FVC ratio, peak expiratory flow (PEF), and forced expiratory flow from 25 to 75% \((FEF_{25–75\%})\) were recorded and expressed as percentages of the expected values in accordance with a subject’s age, height, body weight and gender\(^1\).

Peripheral muscle strength (quadriceps, shoulder abductor and hand grip strength) was evaluated using a hand held digital dynamometer (JTECH, Medical Commander Powertrack II, USA). Measurements were repeated three times on the dominant side\(^1\). The highest value of the measurements was recorded in Newtons (N). The peripheral muscle strength values were expressed as the percentages of predicted values calculated using reference equations\(^7\).

Functional exercise capacity was evaluated using the six-minute walking test (6MWT). The 6MWT was conducted in accordance with American Thoracic Society recommendations\(^1\). For the 6MWT, subjects were asked to walk back and forth along a 30-meter flat corridor as quickly as possible for six minutes. In the pre- and post-test periods, oxygen saturation was measured by a pulse oximeter (KPTS-01, Seoul, Korea). Heart rate, blood pressure, and respiratory rate were also recorded. Pre- and post-test fatigue and dyspnea perception were assessed using the Modified Borg Scale, which is a 0–10 point category scale\(^19\). Upon the completion of the test, the distance covered in the 6-minute walk was recorded in meters. The 6MWT was performed twice, separated an interval of half an hour, on the same day. For each patient, the longer walking distance of the two tests was used in the statistical analysis. The 6MWT distances were expressed as percentages of the expected values for the same age and gender\(^20\).

Postural deformity was evaluated using the postural analysis form developed by Corbin et al. It consists of posterior and lateral observation of the severity of postural deformities. The score is classified as: 0 = none, 1 = mild, 2 = moderate, and 3 = severe\(^21\).

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 18.0 (SPSS Inc., Chicago, USA). Data normality was tested using the Kolmogorov-Smirnov test. Variables are expressed as mean±standard deviation, frequency, and percentages. Student’s t test was used for the comparison of variables showing a normal distribution. The Mann-Whitney U test was used to compare non-parametric variables and those that did not showing a normal distribution. Discrete variables (gender) were compared using the \(\chi^2\) test. Spearman’s rank correlation coefficient was used to investigate associations among the variables. Significance was accepted for values of \(p<0.05\).

Results

The subjects’ characteristics are shown in Table 1. All the children with BPD diagnosis had used oxygen supplementation for more than 28 days. Twelve (66.7%) children with BPD received surfactant and the support of mechanical ventilation in the neonatal period. Birth weight and gestational age were significantly lower in children with BPD than in healthy peers \((p<0.05)\). Age, gender, and body mass of the children with BPD index were similar in the two groups \((p>0.05)\). However, height, body weight, and fat-free mass were significantly lower than those of the healthy subjects \((p<0.05, \text{Table 1})\). No significant difference was found in body fat or percentage of body fat between the children with BPD and the healthy subjects \((p>0.05)\).

The FEV\(_1\), FEV\(_1\)/FVC, PEF, and FEF\(_{25–75\%}\) were significantly lower in the children with BPD than in their healthy peers \((p<0.05, \text{Table 1})\), but FVC was similar between the two groups \((p>0.05)\).

Knee extensor strength and the percentage value of
knee extensor strength were also significantly lower in the children with BPD than in the healthy subjects (p<0.05, Table 2). Knee extensor muscle strength correlated with BMI (r=0.717, p=0.02) in the children with BPD. There were no statistically significant differences in the strength of the shoulder abductor muscles and hand-grip strength between the two groups (p>0.05, Table 2).

The 6MWT distance and %6MWT distance were significantly lower in the children with BPD than in the healthy subjects (p<0.05, Table 2). No statistically significant differences were found between the two groups in the percentage of maximal heart rate reached at the end of 6MWT test, systolic blood pressure, diastolic blood pressure, respiratory rate, dyspnea perception and perception of leg fatigue that were recorded during the test (p>0.05, Table 2).

The lateral, posterior and total scores of analyses of posture were significantly higher in the children with BPD than in the healthy subjects (p<0.05, Table 1). The results show that 55.6% (n=10) of the children with BPD had mild to moderate complication of kyphosis; 33.3% (n=6) had mild to moderate lumbar lordosis; and 22.2% (n=4) had lateral deviation of the spine. Whereas, 25% (n=5) of healthy children had mild kyphosis; 20% (n=4) had mild lumbar lordosis; and 20% (n=4) had mild spinal curvature deviation (p<0.05).

### DISCUSSION

In this study we showed that preterm children with BPD had disturbed pulmonary and extrapulmonary characteristics. The results of this study show that the preterm children with BPD had lower fat-free mass, reduced lung function, worsen postural function, walked a shorter in the 6MWT distance, and had lower quadriceps muscle strength than the healthy children.

Nutritional status, as determined by height, weight, and fat-free mass, is impaired in children with BPD. Premature children with chronic lung disease frequently present delayed growth and under nutrition. Data on the body composition of 6- to 10-year olds is still lacking. It has previously been shown that children with BPD have increased total body water and decreased fat-free mass in the first year of their life (22). Our study is the first study to demonstrate that fat-free mass is still lower than that of healthy controls at 6–10 years of age. Lung infections may lead to decreased energy intake. The medical treatment of preterm BPD, elevated resting metabolic rate, and increased work of breathing have been suggested as causes of the lower growth rates (23–26).

Preterm children with BPD have substantially reduced pulmonary function, a reflection of airway obstruction in the large and small airways which is the cause of significantly lower FEV1, FEV1/FVC, PEF, and FEF25–75%. Most studies have reported lung function impairment in young adults and...
children with BPD. Studies of cystic fibrosis, as a chronic lung disease, have shown that prolonged use of the accessory muscles of respiration and their ensuing hypertrophy, accompanied by a flexed position may result in alterations in body posture, typically increased thoracic kyphosis, chest diameter, shoulder elevation and protraction, and abdominal flexion.

There were some of limitations to this study which should be considered when interpreting the findings. We did not measure the physical activity levels of BPD children; therefore, we did not examine whether their physical activity level contributed to the results. This study was still valuable because it reports postural deformities and reductions in muscle strength for the first time in children with BPD.

In conclusion, we showed that preterm children with BPD had disturbed pulmonary and extrapulmonary characteristics. Their pulmonary function was impaired indicating large and small airway dysfunction. They also had significant postural abnormalities, decreased fat-free mass as well as impaired quadriceps muscle strength, walked a shorter distance in the 6MWT than healthy children. These pulmonary and extrapulmonary features may provide insights for the selection of outcome measures for pulmonary rehabilitation programs for patients with BPD. Interventions for enhancing functional capacity and muscle strength of patients with BPD should be encouraged at an early age.

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