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CARDIO-RESPIRATORY CAPACITY ASSESSMENT IN CHILDREN WITH BRONCHOPULMONARY DYSPLASIA

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ABSTRACT

Objective: To assess cardiorespiratory capacity and investigate the presence of exercise-induced bronchospasm among children with bronchopulmonary dysplasia. Method: Pulmonary function tests and gas analyses were performed in a cardiopulmonary test on 46 children aged 7-10 years. Three groups were formed: children born prematurely with bronchopulmonary dysplasia (BPD; n= 13), children born prematurely without bronchopulmonary dysplasia (Preterm; n= 13) and healthy children born at full term (Control; n= 20). Results: The test duration was 7.70 ± 1.49; 9.1 ± 2.02 and 8.4 ± 2.12 min; VO_2max was 35.98 ± 5.33; 38.99 ± 6.73 and 34.91 ± 6.09 ml/kg/min; and VE was 28.54 ± 7.39; 28.84 ± 5.98 and 28.96 ± 6.96 l/min for the BPD, Preterm and Control groups respectively. There were no significant differences between the groups ($p > 0.05$). The maximum heart rate was 188 ± 9.37; 196 ± 5.15 and 197 ± 10.90 beats/min and the respiratory exchange ratio (RER) was 1.21 ± 0.22; 1.10 ± 0.06 and 1.05 ± 0.05, for the BPD, Preterm and Control groups respectively, and there was a significant difference between the BPD and Control groups ($p < 0.05$). The FEV_1 values before and after exercise were 99 ± 12% and 94 ± 14%; 100 ± 14% and 100 ± 15%; and 102 ± 15% and 101 ± 15%, for the BPD, Preterm and Control groups respectively. Comparison of FEV_1 before and after exercise did not show any significant differences and exercise-induced bronchospasm was not characterized, in any of the groups. Conclusion: The difference in RER may be related to abnormal ventilation and pulmonary diffusion. The cardiorespiratory capacity of children with BPD was similar to that of the Preterm and Control groups.

Key words: chronic neonatal lung disease, children, prematurity, cardiopulmonary test, gas analysis, exercise-induced bronchospasm.

INTRODUCTION

Bronchopulmonary dysplasia (BPD), also referred to as chronic newborn pulmonary disease, was described for the first time in 1967 by Northway et al.[1] in lactating women who had severe hyaline membrane disease, whom were treated with mechanical ventilation and oxygen supplementation. Technological advances and upgrades in care-taking that have occurred in newborn assistance since the 1960s have contributed for the increase in the survival of critically ill pre-term neonates (Pre-term) and the BPD incidence, today known as a disease of the medical progress and one of the most significant sequels originated by the neonate intensive therapy unit[2-4].

The long-term effects on the development of the cardio-respiratory capacity of pre-term newborn with BPD are not yet completely known. Clinical studies are necessary to characterize the long-term development in children, youngsters and adults with BPD. Gas diffusion tests associated to the exercise may provide information about the alveolus-capillary barrier, and spirometry tests may aid to detect abnormalities in the airways, even in non-symptomatic patients[5-7].

Previous studies, that assessed pre-term born children that had BPD at school age, verified that these children use a higher percentage of their ventilatory reserve[8-12], present reductions induced by the exercise in O_2 saturation and increases in trans-dermal CO_2 tension[9,10], when compared with

their controls. In the individual analysis of these children with BPD, alterations were identified on pulmonary functioning and reduction in exercise tolerance[8-12]. Mitchell and Teague have reported reduced gas transportation during rest and exercise in children with BPD and suggest that abnormalities in the pulmonary structure or in the right ventricle dysfunction may justify these findings[13].

Around 25% of the teenagers and youngsters with BPD have reoccurring respiratory symptoms such as pneumonia episodes, hissings and make long-term use of broncho-dilatators, when compared to their controls[8].

It is admitted that the health care received during the peri-natal period might influence the prognosis and the development of pre-term neonates suffering of BPD. In this way, clinical manifestations that are present in Brazilian children may not be comparable to those reported on literature. National data were not found in databases (Lilacs, Scielo, Medline) regarding evolution of these children.

The objective of this study was to evaluate cardio-respiratory capacity and to verify the presence of bronchospasms induced by exercise (BIE) in children between 7 and 10 years of age with BPD, comparing them with pre-term born children (pre-term without BPD) and with healthy children born at full-term and having the same age.

METHODS

The present research was approved by the Ethics in Human Research Committee of the Triângulo University Center – UNITRI and the Uberlândia Federal University – UFU (Process 003/2003). The parents responsible for the children have signed an authorization term for participating in the research after reading an informed consent.

Forty-six children were assessed aged between 7 and 10 year old; they formed three groups: 1) pre-term born children with BPD, BPD group (n= 13); 2) pre-term born children without BPD, Pre-term group (n= 13) and 3) healthy children born at full-term, Control group (n= 20).

Pre-term and BPD children, born between the years of 1993 and 1996, were recruited from lists provided by the Statistical and Medical Archive Service (SMAS) of the UFU's Hospital das Clínicas.

Inclusion criteria for the BPD group (born with gestating clinical age lesser than 37 weeks) were proposed by Bancalari et al.[14]: 1) positive pressure ventilation during the first week of life for at least three days; 2) clinical signs of chronic respiratory disease – tachypnea, respiratory discomfort 3) oxygen supplement necessity for over 28 days in order to keep an oxygen arterial pressure over 50 mmHg or pulse oxymetry over 90%; and 4) trunk radiographies abnormalities, showing persistent grooves in both lungs, alternating with radio-luminescence areas; these formations may coalesce, giving it a bubble aspect.

Twenty-six children had a BPD diagnosis. From these, five evolved to death, four had neurological motor disorders that made impossible their participation in this study, two children did not live in the city of Uberlândia, one child was not found and one did not agree to participate. Thus, 13 children with BPD constituted the totality of children able to participate on this study.

Inclusion criteria for Pre-term group of children were: being born with gestational age lower than 37 weeks, absence of severe respiratory disease at the neonate period and absence of any other chronic disease. The children of the Pre-term group were randomly selected from a list of children provided by SMAS. After the selection, by examining the hospital records, the files of children who evolved to death, the ones who possessed neurological motor disorders, which prevented participation in the study, and the ones that did not reside in Uberlândia city were excluded. The first thirteen children that fulfilled these criteria were selected for the Pre-term group.

The children of the Control group were recruited among the BPD and Pre-term children schoolmates. For this group, the exclusion criterion was the presence of any chronic disease. Data collection was performed in Uberlândia, at the Exercise Laboratory of the UNITRI.

All children responded to a standardized questionnaire, were submitted to a standard clinical assessment, had their weigh and height measured, and performed the pulmonary function test (PFT), according to the Pulmonary Function Tests Guidelines of the Brazilian Society of Pneumology and Tisiology[15]. The reference scores used were the ones by Polgar & Promadhat[16].

For the PFT, a SpiroCard® PC Card flux Spirometer (QRS Diagnostic-Plymouth, USA) was used. A frequencymeter, AXN300 (POLAR-Kempele, Finland), was adjusted to the patient's trunk, who was taken to the cycle-ergometer, Biotec-1800 (CEFISE-Nove Odessa, Brazil), for the necessary adjustments according to his/her biotype. An OxiPuls (FUNDAÇÃO ADIB JATENSE-São Paulo, Brazil) wrist-portable oxymeter was utilized to verify the oxygen peripheral saturation (O_2PS) during the test. The metabolic gas analyzer TEEM-100 (Aerosport/Medgraphics-St Paul, USA) was used for recording and data analysis. To evaluate respiratory discomfort, it was used the Respiratory Discomfort Scale (Brazilian Consensus on Asthma Education[17]).

Data obtained from the participant (age, gender, corporal mass and height) were entered into the metabolic analyzer. A small mouthpiece, connected to the TEEM-100, was adapted to the participant's mouth and fixed by elastic bands, and a nasal clip was also placed onto the participant's nose. An average flux pneumotachometer that operates between 15 to 120 L/min, was connected to the mouth-piece. The metabolic gas analyzer provided, every 20 seconds, the oxygen

consumption values (VO_2), carbonic gas production (VCO_2), VCO_2/VO_2 ratio (gas exchange rate – R), minute ventilation (VE) and heart rate (HR). Maximal HR was calculated as: 210 – (0.65 X age) ± 10%[18].

During the test, a maximum effort protocol was used, with progressive load individualized for every child, based on the protocol proposed by Karila et al.[19]. Individualization of maximum power in watts (W) was based on maximal VO_2 (VO_2max) predicted for each child. Basal VO_2 was calculated according to the equation: (height in centimeters x 2) – 100[19]. The predicted VO_2max was calculated according to the scores proposed by Cooper et al.[20]. From these scores, it was calculated the maximum power, through the equation: Wmax = (predicted VO_2max – basal VO_2 / 10.3. The oxygen equivalent for each power (watts) was 10.3 ml O_2/min/W[19]. The protocol was divided into: a) 3 minutes of rest; b) 3 minutes of warming-up, with an average power of 45% of the predicted maximum; c) approximately 8 minutes of exercise with a 10% increase of the predicted maximum power for each minute until exhaustion and d) 2-3 minutes of cooling-down period with the same power used during warm-up. The exercise time of this protocol lasted for 10-12 minutes (stages "b" and "c").

Power was manually increased on the cyclergometer. The children's parents were allowed to be present during the assessment session, so that the children would feel safer and the parents could encourage them during the test.

The assessment was interrupted when the participant reached exhaustion or when he/she could not keep the right rotation at the cyclergometer (45 RPM), even without having accomplished the proposed protocol. After 10 minutes of the assessment conclusion, it was performed a new pulmonary function test to verify the BIE presence.

For the exercise to be considered maximal, three of the following criteria should be reached: a) participant's exhaustion or incapacity to maintain a rotation higher than 45 RPM, despite verbal encouragement; b) participants reaching the VO_2 plateau (when the final increase of the VO_2 did not exceed 2 mL/kg/min for a 10% load increase) or when the volunteer has reached a score equal or higher than 85% of the predicted VO_2max; c) reaching predicted HRmax or score equal or higher than 90% of the predicted; d) maximal R (Rmax) higher than 1[18].

Results were expressed as average and standard deviation (SD). For all comparisons, significance level was established at α= 0.05. After verifying, through the Shapiro-Wilks test, whether the variables were normally distributed, statistical analysis was performed by parametrical methods. One way Analysis of Variance (ANOVA) was used to compare the three groups, followed by Tukey's test, when appropriate. For the VEF_1 variations, before and after the exercises, it was used the paired t-Student test.

RESULTS

Clinical characteristics, relative to the neonate period of the 26 children of the BPD and Pre-term groups are listed at Table 1. As it can be observed, children of the BPD group presented lower weight and gestational age when compared to the Pre-term group ($p< 0.05$).

Table 1. Neonatal data of children born prematurely (preterm) and children born prematurely with BPD (BPD).

Group	BW *(grams)*	GA *(weeks)*	MV *(Days)*	O_2 *(Days)*	PHA *(Days)*
BPD	1037* ± 229	32* ± 1.5	11* ± 6.6	48* ± 22.5	79* ± 18
	(830-1670)	(30-34 e 4/7)	(3-26)	(28-102)	(44-106)
Pré-term	1765 ± 621	35 ± 2.3	1 ± 2	4 ± 4	29 ± 25
	(850-2800)	(28-36 e 5/7)	(0-6)	(0-10)	(2-76)

BW: birth weight; GI: gestational age; MV: mechanical ventilation; O_2: oxygen supplementation; LHS: length of hospital stay. Values are expressed as arithmetic mean (M) ± standard deviation (SD) and range (minimum-maximum). * P< 0.5.

Table 2. Demographic and anthropometric data of the BPD, Pre-term and Control groups.

Group	N	Gender	Age *(years)*	Height *(cm)*	Weight *(kg)*	BMI *(Weight/height^2)*
BPD	13	9M/4F	8.5 ± 0.97	129.9 ± 7.31	26.0 ± 5.84	15.3 ± 2.25
Pre-term	13	8M/5F	8.3 ± 1.11	131.2 ± 7.32	28.6 ± 9.49	16.4 ± 3.92
Control	20	9M/11F	8.2 ± 1.14	133.9 ± 7.99	30.1 ± 9.10	16.5 ± 3.29

BMI, body mass index. Results expressed as mean ± standard deviation (SD).

Table 2 presents the demographic and anthropometrical characteristics of the children. Despite the fact that the BPD group presented slightly lower scores of weight, height and CMI in relation to the Pre-term and Control groups, these differences did not reach statistical significance levels.

According to questionnaire answered by the participant's guardians, eight children (17.40% of the total children) reported some sort of discomfort triggered by the exercise (lack of air, thoracic pain). Four of these belonged to the BPD group (30.76% of the group) and four to the Pre-term group (30.76%), while no discomfort was reported on the Control group.

All children from the BPD group had the effort test considered maximal, however, 3 children on the Pre-term group (23%) and 3 children on the Control group (15%) did not reach the proposed criteria for the exercise to be considered maximal. Thus, these children were excluded from the analyses.

Pre-exercise and post-exercise VEF_1 scores for the groups were: BPD group 99 ± 12% and 94 ± 14%; Pre-term group 100 ± 14% and 100 ± 15%; and Control group 102 ± 15% and 101 ± 15%. The variation of these scores did not show significant differences in any group. However, an individualized analysis demonstrated that one child of the Pre-term group and two children of the BPD group presented > 10% VEF_1 reduction characterizing BIE, representing 6.5% of all children that participated of the research.

Only one child, whom belonged to the BPD group, presented moderate respiratory discomfort during the assessment, characterized by thoracic pain and presence of hissing on the pulmonary auscultation immediately after the assessment's interruption. The discomfort ceased after ten minutes. No cardiorespiratory complication was observed on the children during the test, indicating a good tolerance to the proposed protocol.

Mean test duration for the children of the BPD group was 7.7 ± 1.49 minutes, for the Pre-term group was 9.1 ± 2.02 minutes, and for the Control group it was 8,4 ± 2,12 minutes. No significant difference was found among the groups.

Ten children (77%) of the BPD group, 10 children (77%) of the Pre-term group and 17 children (85%) of the Control group have reached HRmax predicted in beats per minute. HRmax for the three groups have showed that scores of the BPD group were significantly lower than the observed on the Control group. All groups obtained a mean HRmax higher than 90% of the predicted HRmax (Table 3).

Significant differences were not found on the scores of VO_2max, maximal power reached in relation to the maximal predicted power and VE among the groups, which suggests that they are not different, regarding cardiorespiratory capacity (Table 3). The Rmax analysis for the three groups demonstrated that scores of the BPD group were significantly higher than the ones observed on the Control group (Table 3).

DISCUSSION

This study is, possibly, the first study made in Brazil that demonstrates the cardio-respiratory condition of children at school age who were born pre-term with and without BPD diagnosis, due to the fact that it was not found, in scientific literature databases, a similar national study.

It is common the report of exercise discomfort in children that were born pre-term with or without BPD, and, sometimes, this reported discomfort comes accompanied by BIE[5,8,9]. In the present study, it was investigated the presence of respiratory discomfort triggered by exercise. Considering both the Pre-term and BPD groups, the adults responsible for 8 children reported respiratory problems such as lack of air and repeating infections.

The VEF_1 scores comparison before and after the exercise, on the three studied groups, did not present significant differences. However, an individualized analysis has demonstrated that one child of the Pre-term group and two children of the BPD group presented a VEF_1 reduction >10%. According to Anderson[21], VEF_1 reductions > 10% characterizes BIE. In this sense, it is noteworthy the presence of BIE in children of these groups. Similar results are described by Bader et al.[9] and Mitchell & Teague[13]. Although in both

Table 3. Cardiopulmonary exercise test - Individualized Protocol for Workload Increase.

Group	VO_{2max} *(L/min)*	VO_{2max} *(ml/Kg/min)*	VO_{2max} *(%pred)*	HR_{max} *(beats/min)*	HR_{max} *(%pred)*	RER *(VCO_2/VO_2)*	VE_{max} *(L/min)*	W_{max} *(Watt)*	W_{max} *(%pred)*
BPD (n= 13)	0.94 ± 0.26	35.98 ± 5.33	96 ± 15.00	188* ± 9.37	92* ± 4.50	1.21* ± 0.22	28.54 ± 7.39	88.60 ± 18.55	97 ± 15.50
Preterm (n= 10)	1.00 ± 0.20	38.99 ± 6.73	103 ± 18.22	196 ± 5.15	96 ± 2.62	1.12 ± 0.06	28.84 ± 5.98	93.38 ± 18.71	107 ± 19.95
Control (n= 14)	1.04 ± 0.18	34.91 ± 6.09	91 ± 18.12	197 ± 10.90	96 ± 5.25	1.06 ± 0.05	28.96 ± 6.96	90.79 ± 23.68	91 ± 24.07

RER, respiratory exchange ratio. Results expressed as mean ± standard deviation.

studies the average scores of the groups have not reached the established levels for BIE, these scores clearly indicate BIE presence in some children. Gross et al.[22] reported that 19% of the BPD group and 9% of the Pre-term group presented VEF_1 < 60% of the predicted after the effort assessment, indicating moderate obstruction of the airflow. Since the VEF_1 reduction has not been assessed, at the present study, it was not possible to estimate BIE incidence[22]. However, the results described by these authors and the obtained at the present study show that Pre-term children with or without BPD may present broncho-spasms during physical activity.

One child (8%) of the BPD group presented moderate respiratory discomfort during assessment. Mitchell & Teague[13] reported that five children (50% of their sample) presented some sort of respiratory discomfort during the maximum effort assessment. Pianosi & Fisk[12] reported that, apparently, no child of their study presented respiratory discomfort during the test. In addition to weight at birth, gestational age and time of oxygen supplementation and mechanical ventilation, other factors such as abnormalities on the mechanics and/or ventilatory efficiency and gas diffusion may determine intolerance to exercise in children with chronic pulmonary diseases[23]. These disparities are probably due to differences on the severity of respiratory impairment caused by BPD in children that participated of these studies.

No cardio-respiratory complication was observed during assessment, indicating a good tolerance to the proposed protocol. Utilization of this protocol, with individualized increasing of the predicted load for each child, may have favored the test's acceptability by the children. Other protocols with non-individualized load increase may lead to premature interruption of the exercise before the child reaches the predicted cardiac and respiratory indexes due to fatigue of the lower limbs muscles[23]. The Average time length of the tests was enough so that it was possible to perform the maximum effort test. According to the European Respiratory Society the maximum effort test is "a test that makes it possible the integration and exploration of the pulmonary, cardiac and muscular systems, in certain conditions in which the body consumes its reserves"[24]. Most children from the present study performed the maximal effort assessment, which supports the applicability of the loads of this protocol.

VO_2max scores obtained by the three groups, in our study, are similar to those obtained in previous studies performed in healthy children, or in children that presented respiratory diseases, abnormal symptoms during exercise, complex cardiopathies treated surgically, bronchopulmonary dysplasia, and others disorders[6,10,12,19]. The results found at the present study are similar to those described by Jacob et al.[10], who also did not encounter significant differences on the VO_2max reached by children with BPD, pre-term without BPD and healthy children born at full-term. Kilbride, Gelatt and Sabath[6] described distinct results, while assessing cardiorespiratory capacity of children and pre-teenagers between 9 and 15 years of age. These authors reported VO_2max scores significantly lower on the pre-term groups with and without BPD, when compared to the group of healthy children born at term. It is possible that these differences are due to clinical characteristics of the neonate period of the assessed children. In fact, the pre-term groups (with and without BPD) had gestational age of 26 weeks, weight at birth of 700g, duration of mechanical ventilation of 38 days, and O_2 supplement of 73 days, comprising a sample of greater clinical severity than the sample assessed at the present study.

HRmax was reached by most of the children (80%), but, while observing each children individually, it was observed that a greater percentage of children from the Control group (85%) has reached HRmax, in relation to the BPD and Pre-term (77%). Determining HR during the effort assessment is necessary, since HRmax is one of the most reliable criterion for determining the maximal effort and presents strong correlation with VO_2max[19].

Rmax was significantly higher for the BPD group than for the Control group. One R-value greater than 1.0 may be caused by the CO_2 originated from the lactic acid or from a hyperventilation. CO_2 has a greater solubility on the tissues when compared to O_2. Thus, in effort assessments, both lactic acidosis and hyperventilation must be taken in account[25,26]. In this sense, it can be deducted that children with BPD presented a higher level of lactic acidosis, with greater lactic acid formation so that they could keep exercising, indicating that the O_2 income was enough for the demand[24,25]. The O_2 income may have been lower when compared to their controls[12,13,23,26,27], which may have interfered on the O_2 capture and, consequently, in higher R scores.

This study has found similar between group results, in relation to exercise tolerance or to the cardio-respiratory response to the exercise, which agree with most studies with pre-term children, with or without BPD, that are at school age[3,8,10,12,13,22,23,27].

In the present study, there is a lack of socio-economical characterization and classification of physical activity level of the children, which could allow a more detailed sample matching. Thus, the absence of quantitative data of the control group children was one of the study limitations.

Previous studies suggest that even discrete alterations of the pulmonary functioning, at childhood, may be precursors of chronic pulmonary disease at adult stage, and the progression of pulmonary function loss on the BPD suffering individuals is yet unknown[8]. Longitudinal studies are necessary to better describe pulmonary evolution of these assessed children and to provide a prediction of how could their pulmonary conditions be in the future.

On the Physical Therapist, Pneumologist, and Pediatrician's perspective, children with BPD that reach teenage and adult age are a new group of patients that require greater attention, through special programs, aiming smoking prevention, the incentive of regular sport practice, and with

structured programs of pulmonary rehabilitation and regular clinical follow-up.

The proposed protocol has demonstrated to be safe, with good clinical tolerance from the BPD children, who demonstrated good acceptability to the proposed exercise, without evidences of abnormalities or cardio-vascular limitation. Thus, this protocol may be used in assessments with children for diagnosis, treatment prescription, and follow-up of the pathology progress.

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REFERENCES

1. Northway WHJ, Rosan RC, Porter DY. Pulmonary disease following respirator therapy of hyaline-membrane disease. Bronchopulmonary dysplasia. N Engl J Med. 1967;276:357-68.
2. Coalson JJ. Pathology of new bronchopulmonary dysplasia. Semin Neonatol. 2003;8:73-81.
3. D'Angio CT, Maniscalco WM. Bronchopulmonary dysplasia in preterm infants: pathophysiology and management strategies. Paediatr Drugs. 2004;6:303-30.
4. Perez Perez G, Navarro Merino M, Romero Perez MM, Saenz Requera C, Pons Tubio A, Polo Padillo J. Respiratory morbidity after hospital discharge in premature infants born at < or = 32 weeks gestation with bronchopulmonary dysplasia. An Pediatr (Barc). 2004;60(2):117-24.
5. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2001;163:1723-9.
6. Kilbride HW, Gelatt MC, Sabath RJ. Pulmonary function and exercise capacity for ELBW survivors in preadolescence: effect of neonatal chronic lung disease. J Pediatr. 2003;143:488-93.
7. Matecki S, Paruit C, Chaussain M, Ramonatxo M, Denjean A; Groupe EFR pediatriques de la Societe de Physiologie. Indications and application of exercise tests in children. Rev Mal Respir. 2001;18:491-8.
8. Eber E, Zach MS. Long term sequelae of bronchopulmonary dysplasia (chronic lung disease of infancy). Thorax. 2001; 56:317-23.
9. Bader D, Ramos AD, Lew CD, Platzker AC, Stabile MW, Keens TG. Childhood sequelae of infant lung disease: exercise and pulmonary function abnormalities after bronchopulmonary dysplasia. J Pediatr. 1987;110(5):693-9.
10. Jacob SV, Lands LC, Coates AL, Davis GM, MacNeish CF, Hornby L, et al. Exercise ability in survivors of severe bronchopulmonary dysplasia. Am J Respir Crit Care Med. 1997;155(6):1925-9.
11. Parat S, Moriette G, Delaperche MF, Escourrou P, Denjean A, Gaultier C. Long-term pulmonary functional outcome of bronchopulmonary dysplasia and premature birth. Pediatr Pulmonol. 1995;20(5):289-96.
12. Pianosi PT, Fisk M. Cardiopulmonary exercise performance in prematurely born children. Pediatr Res. 2000;47:653-8.
13. Mitchell SH, Teague WG. Reduced gas transfer at rest and during exercise in school-age survivors of bronchopulmonary dysplasia. Am J Respir Crit Care Med. 1998;157:1406-12.
14. Bancalari E, Abdenour GE, Feller R, Gannon J. Bronchopulmonary dysplasia: clinical presentation. J Pediatr. 1979; 95(5 Pt 2):819-23.
15. Pereira CAC, Neder JA. Diretrizes para testes de função pulmonar. J Pneumol. 2002;28 Suppl 3:S1-238.
16. Polgar G, Promadhat V. Pulmonary function testing in children: technics and standards. W.B. Saunders 1971; Philadelphia: p. 42-212.
17. Sociedade Brasileira de Pneumologia e Tisiologia; Sociedade Brasileira de Pediatria; Sociedade Brasileira de Alergia e Imunopatologia. Consenso Brasileiro De Educação Em Asma I. J Pneumol. 1996; 22 Suppl 1:S1-24.
18. Wasserman K, Hansen JE, Sue DY, Whipp BJ, Casaburi R. Priciples of exercise testing and interpretation. 2ªed. Philadelphia: Lea & Febiger; 1994.
19. Karila C, de Blic J, Waernessyckle S, Benoist MR, Scheinmann P. Cardiopulmonary exercise testing in children: an individualized protocol for workload increase. Chest. 2001;120(1): 81-7.
20. Cooper DM, Weiler-Ravell D, Whipp BJ, Wasserman K. Aerobic parameters of exercise as a function of body size during growth in children. J Appl Physiol. 1984;56(3):628-34.
21. Anderson SD. Exercise-induced asthma in children: a marker of airway inflammation. Med J Aust. 2002;(177 Suppl):S61-3.
22. Gross SJ, Iannuzzi DM, Kveselis DA, Anbar RD. Effect of preterm birth on pulmonary function at school age: a prospective controlled study. J Pediatr. 1998;133:188-92.
23. Baraldi E, Bonetto G, Zacchello F, Filippone M. Low exhaled nitric oxide in school-age children with bronchopulmonary dysplasia and airflow limitation. Am J Respir Crit Care Med. 2005;171:68-72.
24. European Respiratory Society Task force on standardization of clinical exercise testing. Clinical exercise testing with reference to lung disease: indications, standardization and interpretation strategies. Eur Respir J. 1997;10:2662-89.
25. American Thoracic Society. Pulmonary rehabilitation. Am J Respir Crit Care Med. 1999;159:1666-82.
26. Parker TA, Abman SH. The pulmonary circulation in bronchopulmonary dysplasia. Semin Neonatol. 2003;8:51-61.
27. Abman SH. Monitoring cardiovascular function in infants with chronic lung disease of prematurity. Arch Dis Child Fetal Neonatal Ed. 2002;87:F15-8.