Actividad electromiográfica de los músculos respiratorios en bebés prematuros con displasia broncopulmonar: un estudio longitudinal

Electromyographic activity of respiratory muscles in premature infants with bronchopulmonary dysplasia: a longitudinal study

Rosa TR[a], Sepúlveda-Loyola W[a, b], Soares DS[a, c, d, e], Kreling JC[d], Felcar JM[a, c, f], Ferrari LSL[d, g], Silva-Junior RA[a, h], Krueger E[a, i], Probst VS[a, c, f]

[a] UEL-UNOPAR Associate Graduate Program in Rehabilitation Sciences, Londrina State University (UEL), Pitágoras University (UNOPAR), Londrina, PR, Brazil

[b] Faculty of Health and Social Science, Universidad de Las Américas, Santiago, Chile

[c] Movement Sciences Laboratory, Specialized Center of Research and Postgraduation in Health Studies (CEPPOS); Health Sciences Center, State University of Londrina (UEL), Londrina-PR, Brazil

[d] Neonatal Intensive Care Unit, University Hospital, Londrina State University (UEL), Londrina, PR, Brazil

[e] Hospital Infantil Albert Sabin, Fortaleza CE, Brazil

[f] Department of Physiotherapy, Health Sciences Center (CCS), Londrina State University (UEL), Londrina, PR, Brazil

[g] Department of Pediatrics and Pediatric Surgery, Health Sciences Center (CCS), Londrina State University (UEL), Londrina, PR, Brazil

[h] Faculty of Health Sciences, Universidades McGill and UQAC (Saguenay Québec), Canada

[i] Department of Anatomy, Center for Biological Sciences (CCB), Londrina State University (UEL), Londrina, PR, Brazil

Correspondencia:
Walter Sepúlveda-Loyola
wsepulveda@udla.cl

Recibido: 8 febrero 2024
Aceptado: 20 marzo 2024

RESUMEN

Introducción: falta evidencia sobre el estado del tono de los músculos respiratorios en bebés prematuros con displasia broncopulmonar DBP realizada con mediciones objetivas. *Objetivo*: evaluar el tono muscular de los músculos inspiratorios accesorios en bebés prematuros con y sin DBP desde el nacimiento hasta las 36 semanas de gestación. *Material y método:* estudio clínico observacional longitudinal con 37 recién nacidos prematuros de menos de 36 semanas de edad gestacional y peso menor a 1.500 gramos, hospitalizados en la unidad de cuidados intensivos neonatales. Los bebés prematuros fueron sometidos a evaluaciones del tono muscular con electromiografía de superficie cada 2 semanas después del nacimiento, en los músculos: pectoral mayor, serrato anterior, trapecio y erector de la columna. Se excluyeron aquellos con complicaciones graves, muertes y menos de 3 medidas de electromiografía de superficie. Los bebés prematuros se asignaron a 2 grupos: bebés prematuros con displasia broncopulmonar (con DBP, definida por la necesidad de oxígeno suplementario durante 28 días o más) y grupo de control, sin DBP. *Resultados:* los prematuros con displasia broncopulmonar presentaron mayor tono muscular en trapecio en la 1ª, 2ª, 3ª y 4ª evaluación, en el serrato anterior sólo en la 1ª evaluación y en erector de la columna en la 2ª y en la 4ª evaluación, en comparación con el GC ($p < 0,05$ para todos). En el análisis intragrupo, el tono muscular del erector de la columna disminuyó con el tiempo en ambos grupos ($p < 0,05$). Además, los bebés con DBP requirieron más soporte ventilatorio invasivo y no invasivo en comparación con el GC ($p < 0,05$ para todos). *Conclusión*: los bebés prematuros con DBP exhiben un mayor tono muscular en los músculos inspiratorios accesorios y una elevada necesidad de soporte ventilatorio durante la hospitalización en la unidad de cuidados intensivos neonatales.

Palabras clave: displasia broncopulmonar, tono muscular, electromiografía de superficie, recien nacido prematuro.

ABSTRACT

Introduction: *there is a lack of evidence with objective measurements of respiratory muscle tone in premature infants with bronchopulmonary dysplasia BPD.* Objective: t*o assess the muscle tone of accessory inspiratory muscles in premature infants with and without BPD from birth to 36 gestational weeks*. Material and method: *a longitudinal observational clinical study with 37 premature infants of less than 36 weeks of gestational age and weighing less than 1500 grams, hospitalized at the neonatal intensive care unit. Premature infants underwent assessments of muscle tone with surface electromyography every two weeks after birth, on the muscles: pectoralis major, anterior serratus, trapezius, and erector of the spine. Those with severe complications, deaths and fewer than three surface electromyography measures were excluded. Premature infants were allocated into two groups: premature infants with bronchopulmonary dysplasia (with BPD, defined by the need for supplemental oxygen for 28 days or more) and control group, without BPD.* Results: *premature infants with bronchopulmonary dysplasia presented higher muscle tone in trapeziusin the 1st, 2nd, 3rd and 4th evaluations, in anterior serratus only in the 1st evaluation and inerector of the spine in the 2nd and in the 4th evaluations, compared to CG ($p < 0.05$ for all). In the intragroup analysis, the muscle tone of erector of the spine decreased over time in both groups ($p < 0.05$). In addition, infants with BPD required more invasive and non-invasive ventilatory support compared to CG ($p < 0.05$ for all).* Conclusion: *premature infants with BPD exhibit heightened muscle tone in accessory inspiratory muscles and elevated requirement for ventilatory support during the hospitalization in the neonatal intensive care unit.*

Keywords: *bronchopulmonary dysplasia, muscle tonus, surface electromyography, premature infants.*

DATA AVAILABILITY

The data used to support the results of this study are included within the article. The data are available from the corresponding author upon reasonable request and with permission of the Research Group of the Health Sciences Center, State University of Londrina, Londrina-PR, Brazil.

INTRODUCTION

Numerous advances in neonatal care, have provided an expressive increase in the rate of survival in preterm newborns (PTB). Modest reductions in the incidence of several comorbidities of prematurity have also accompanied these improved practices, with the exception of bronchopulmonary dysplasia (BPD) incidence, which has remained steady or increased over time depending on country/geographic region[1].

The etiology of BPD has not been fully established; its origin is related to multiple factors. BPD is associated with lower gestational age and lower birth weight, patent ductus arteriosus, late-onset sepsis, use of surfactant, need for mechanical ventilation and duration of mechanical ventilation. Furthermore, an association was observed between patients with intrauterine growth restriction and those born with less than 32 weeks of gestational age (GA). One of the definitions of BPD considers mild BPD infants who had received oxygen or respiratory support for > 28 days but were on room air at 36 weeks GA[2]. Babies with moderate BPD: required supplemental oxygen with a fraction of inspired oxygen (FiO_2) concentration < 30 %, at 36 weeks of GA. Finally, severe BPD was classified as use of > 30 % oxygen or positive pressure at 36 weeks[2]. The prevalence range varies from 20 to 40 %, according to the population studied, neonatal care and diagnostic criteria[3-5].

Young adults with BPD have chronic lung disease characterized by airflow obstruction, intermittent pulmonary exacerbations and worse pulmonary function[5-7]. Previous evidence suggests that in children with BPD, disrupted lung development, genetic susceptibility, subsequent environment, and infectious events that occur during critical periods of postnatal lung development could increase the predisposition of early onset chronic

obstructive pulmonary disease (COPD)[7]. It is known that individuals with COPD present changes in lung function that not only over activates accessory respiratory muscles but also increases the burden on respiratory muscles[8], which has been studied in preterm infants[9].

The muscle activity can be evaluated subjectively, during physical examination with the use of scales, and objectively, by surface electromyography (EMG), which is a technique to assess the electrical activity produced by a muscle, with electrodes positioned on the surface of the skin[10-12]. EMG has already been used in the infant's population to assess upper and lower limb muscle tone[13, 14] and to evaluate the effectiveness of the Kangaroo method[15-17]. However, in infants with BPD the respiratory muscle activity has not been studied yet.

Recent studies[18, 19] have already demonstrated that EMG is capable of monitoring breathing in premature babies and detecting changes in diaphragm activity over time following changes in the mode or level of respiratory support. The study by Van Leuteren et al. shows a modest but variable difference between the work of breathing and diaphragm activity, measured with transcutaneous electromyography, in premature babies using nasal CPAP and suggests that studies need to confirm this finding in a larger group of babies with more significant lung disease[18]. Considering the importance of the tone of the accessory inspiratory muscles in infants and the lack of evidence in those with BPD, this study aimed to objectively assess the tone of the accessory inspiratory muscles in infants with and without BPD from birth to 36 weeks of gestational age (GA).

MATERIAL AND METHOD

Study design

A longitudinal observational clinical study following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE), with infants hospitalized at the Neonatal Intensive Care Unit (NICU) at the University Hospital of Londrina, Paraná, Brazil. Infants were allocated into two groups, with BPD (BPDG) and without BPD, control group (CG). BPD was diagnosed as preterm newborns who needed supplemental O_2 with a fraction of inspired oxygen (FiO_2) greater than 0.21 for 28 days or more[4]. The study was approved by the Ethics Committee in Research of the Londrina State University (number 1.316.581). This study is part of a Master thesis registered in the platform of the UEL-UNOPAR Associate Graduate Program in Rehabilitation Sciences, Londrina State University (UEL), Pitágoras University (UNOPAR), Londrina, PR, Brazil[20].

As the objective was to compare the muscle tone of children with BPD with children who did not develop BPD, it was decided to include moderate and late premature babies (32 to 37 incomplete weeks of gestation) and not just very premature babies (28 to 32 incomplete weeks). and extremely premature – gestational age less than 28 weeks. The inclusion criteria were: preterm infants with GA less than 36 weeks and birth weight less than 1500 g; respiratory rate between 40 and 60 rpm, heart rate between 120 and 160 bpm, peripheral oxygen saturation lower than 89 %, absence of cyanosis, pallor or pain (assessed by Neonatal Infant Pain Scale); absence of perinatal asphyxia (Apgar < 4 in the fifth minute of life, metabolic acidosis or mixed acidemia -pH < 7.00- and clinical neurological sequelae in the immediate neonatal period)[21] and absence of congenital malformations and genetic syndromes.

Preterm infants with grade IV periventricular hemorrhage, periventricular leukomalacia, postoperative hemorrhage that interfered at the time of evaluation or use of drugs which interfere in the state of consciousness at the time of the evaluation and also those infants with less than three electromyographic evaluations (to ensure longitudinal monitoring of muscle tone) were excluded.

Procedures

Muscle tone was assessed in infants by surface EMG with an eight-channel surface electromyography (model EMG 830C, EMG System do Brazil Ltda, São José dos Campos, São Paulo, Brazil). To allow electrode-skin contact, the area of the skin was cleaned with distilled water. Electromyographic signals were collected through two disposable surface electrodes associated with a conductive gel (model MSGST-06, Solidor, Medico Eletrodes International Ltda., Noida, Uttar Pardesh, India).

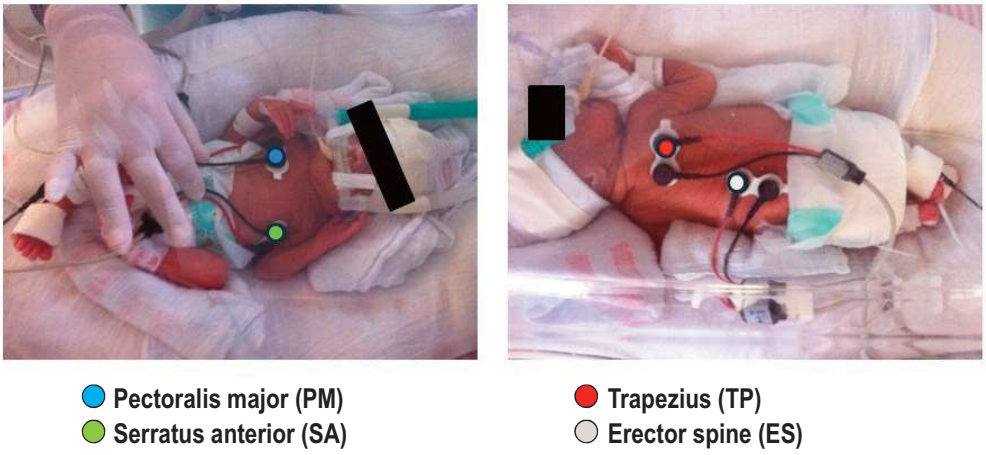

FIGURE 1. **Reference points for surface ElectroMiography for the Non-Invasive Assessments of Muscles.**

These were positioned, with a distance of 20 mm between them, in the following muscles: anterior serratus (AS), pectoralis major (PM), trapezius (TP) and erector spine (EE), according to the standardization of Surface Electro Miography for the Non-Invasive Assessments of Muscles (SENIAM)[22] and the reference electrode in the lateral malleolus of the lower limb free of venous accesses or sensors (figure 1).

Evaluations were performed by trained physical therapists during food administration intervals. Infants who met inclusion criteria were assessed from the first week of admission. Those infants who presented clinical instability on the first week of life or weighted less than 1000 g and/or has 28 weeks of GA or less were evaluated on the second week after birth due to minimal handling protocol of the unit (BPDG: n = 18 and CG: n = 6). All infants included were re-evaluated every two weeks until 36 weeks of GA.

PTB who needed supplemental O_2 for 28 days or more were identified as BPDG and those who did not require O_2 supplementation were allocated into the control group (CG). With respect to the BPDG, babies in this group were classified as having mild, moderate or severe BPD according to severity criteria[4].

Initially, electromyographic evaluation was performed with the baby positioned in dorsal decubitus with the electrodes placed in the unilateral PM and unilateral AS muscle, and the electromyographic signals were simultaneously captured for two minutes. Then, the baby was positioned in ventral decubitus with abdominal support through a diaper and, after accommodation in the posture, the signals of the TP muscles -unilateral medium fibers and unilateral EE- were captured for other two minutes. During the evaluations the babies remained at rest, awake and quiet (scores between 3 and 5 on the Brazelton scale)[23].

The signals were captured and converted into digital signals. Out of the 2 minutes captured, the first and last 30 seconds were deleted. Therefore, out of the 60 remaining seconds, only 20 seconds were analyzed using the Matlab program (MathWorks Inc; Natick, Massachusetts, USA). The third-order Butterworth filter was used, with a bandpass of 20 to 450 Hz with a filter rejection band at 60 Hz and harmonics, and then recorded the median frequency (Hz) and the root mean square (RMS) in Volts.

To minimize the adverse effects of the environment, the heated incubator was switched off at the time of signal pickup and if the baby was in phototherapy, it was also switched off.

Statistical analysis

For statistical analysis, the software Graph Pad Prism 6.0 (GraphPad Software Inc, San Diego, California, USA) and Excel 2010 (Microsof Office; Redmond, Washington, USA) were used. The normality distribution analysis was performed by the Shapiro-Wilk test and the data were

described in percentages and in mean ± standard deviation, according to the normality test. The evaluation of intragroup changes over time was analyzed using the repeated measures ANOVA test. Intergroup differences were analyzed using the unpaired or paired t-test. Measurements of proportion between groups were analyzed using the chi-square test or Fisher's exact test. Outliers were excluded (values greater or less than 1.96 standard deviation from the mean)[22] for the analysis. The statistical significance adopted was $P < 0.05$.

RESULTS

Seventy-three premature infants (GA < 36 weeks and PN < 1500 g) were born in the period from May 2016 to February 2017, being 52 infants included. The flowchart of the study is presented in figure 2. Weight, GA, Apgar, FiO_2 used during resuscitation in the delivery room and during the first 24 hours of life, mechanical ventilation and length of stay in the groups studied, are presented in table 1.

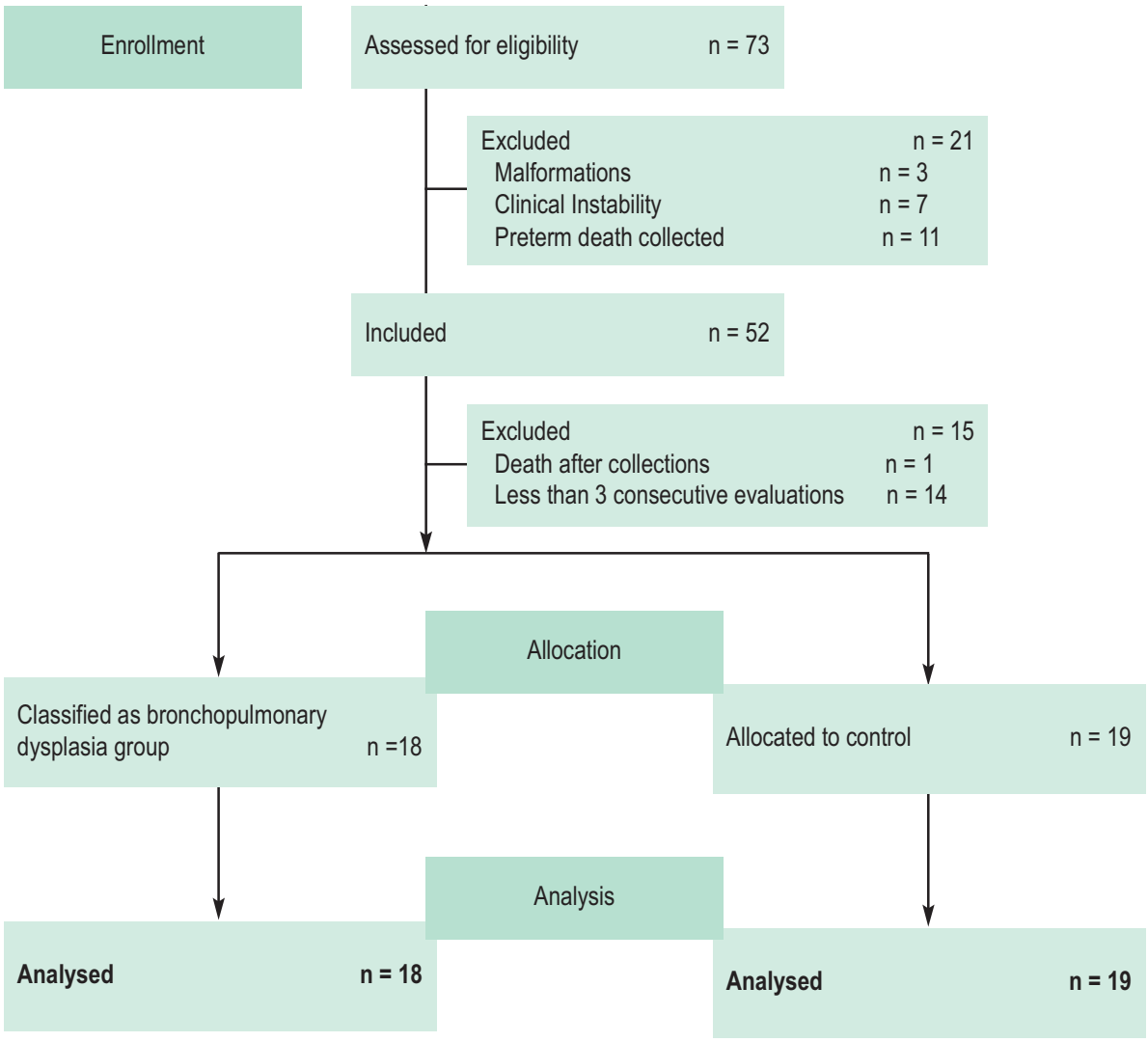

FIGURE 2. **Consolidated Standards of Reporting Trials (CONSORT) flow chart for trial recruitment.**

TABLE 1. **Characterization of the groups.**

Variables	BPDG (n = 18)	CG (n = 19)	P
Weight (g)	882.5 ± 54.3	1200 ± 47.7	< 0.0001*
GA (weeks)	26.7 ± 0.4	30 ± 0.4	< 0.0001*
Apgar 1st minute	3.9 ± 0.73	5.9 ± 0.6	0.039*
Apgar 5th minute	7.5 ± 0.3	8.7 ± 0.2	0.010*
Apgar 10th minute	9.3 ± 0.3	9.8 ± 0.1	0.14
FiO_2 resuscitation (%)	60 ± 10	50 ± 9	0.36
MIV (days)	22.1 ± 4.7	3.1 ±1.6	0.0004*
NIPPV (days)	11.3 ± 1.9	4.3 ± 1.0	0.0018*
CPAP (days)	8.5 ± 1.5	5.3 ± 1.1	0.09
O_2 inhalation (days)	19.8 ± 2.6	2.7 ± 0.9	< 0.0001*
FiO_2 in the first 24 hours (%)	70 ± 6	50 ± 6	0.042*
Length of stay (days)	83.3 ± 5.7	51.8 ± 4.5	0.0001*

GA: gestational age; FiO_2 max: fraction of inspired oxygen; MIV: Mechanical Invasive Ventilation; NIPPV: Nasal Intermittent Positive Pressure Ventilation; CPAP: continuous positive airway pressure; O_2 inhalation: inhaled oxygen.

Regarding to the ventilatory assistance received by the infants, BPDG used more invasive mechanical ventilation (IMV) in the first 24 hours of life compared to CG (94 % versus 37 %, P = 0.0004), less non-invasive ventilation (44 % versus 79 %, P = 0.04) and required more exogenous surfactant (72 % versus 32 %, P = 0.01). Only BPDG received hydrotherapy during the period of NICU stay (72 % versus 0 %, P < 0.0001).

The information about the days of life, weight, GA and FiO^2 in the different moments of the electromyographic evaluations in both groups, is presented in table 2. BPDG presented greater need for orotracheal tube replacement (39 % versus 5 %, P = 0.01), number of accidental extubations (44 % versus 11 %, P = 0.02) and extubation failure (considered a return to IMV less than 48 hours after extubation) (67 % versus 0 %, P < 0.001) compared to CG. In the BPDG, 10 premature infants presented mild (56 %), moderate (38 %) and severe (5 %) BPD.

The results of the electromyographic evaluations are described in table 3. BPDG presented higher muscle tone of AS, TP and EE compared to the CG. The intragroup analysis showed that EE presented a decrease in muscle tone over time (P < 0.05) in both groups. Correlations were run between muscle tones of all muscles with GA variables, weight, kind of ventilatory support used in each EMG evaluation, ventilatory parameters and BPD severity. In BPDG, only the positive pressure was correlated with the muscle tone of TP in the second evaluation (r = -0.64, P = 0.01), the FiO_2 with TP in the fourth evaluation (r = 0.68, P = 0.02). And the severity of BPD showed a significant correlation with positive pressure in the second EMG evaluation (r = 0.60; P = 0.03).

TABLE 2. **Characteristics of groups studied at the time of electromyographic evaluations.**

	1st EMG Ev.			2nd EMG Ev.		
Variables	**BPDG (n = 18)**	**CG (n = 19)**	**P**	**BPDG (n = 18)**	**CG (n = 19)**	**P**
Weight (g)	905 ± 58	1155 ± 42	0.001*	1068 ± 66	1413 ± 61	0.0005*
GA (w)	28.5 ± 0.35	31 ± 0.3	<0.0001*	30.5 ± 0.35	33 ± 0.3	< 0.0001*
DL (days)	13 ± 0.6	7 ± 0.5	<0.0001*	27 ± 0.8	21 ± 0.8	< 0.0001*
FIO_2 (%)	36 ± 3	22 ± 6	0.002*	35 ± 3	22 ± 6	0.0002*
	3rd EMG Ev.			**4th EMG Ev.**		
Variables	**BPDG (n = 18)**	**CG (n = 19)**	**P**	**BPDG (n = 18)**	**CG (n = 19)**	**P**
Weight (g)	1290 ± 72	1696 ± 82	0.0008*	1530 ± 83	1808 ± 112	0.06
GA (w)	32.6 ± 0.35	35 ± 0.3	<0.0001*	34.3 ± 0.35	35.6 ± 0.25	0.02*
DL (days)	41 ± 0.9	35 ± 1	0.0001*	54 ± 0.9	50 ± 1.9	0.06
FIO_2 (%)	36 ± 4	21 ± 0	0.01*	30 ± 3	21 ± 0	0.13

EMG Ev.: electromyographic evaluation; CG: control group; BPDG: bronchopulmonary dysplasia group; GA: gestational age; w: weeks; DL: days of life; FIO_2: fraction of inspired oxygen; # n = 8; *significance difference P < 0.05.

DISCUSSION

The present study observed that the electromyographic activity of accessory inspiratory muscles in premature infants with BPD is greater compared to those without this disease. In this line, three of four muscles evaluated presented greater muscle tone in premature infants with BPD compared to control group.

Pulmonary diseases such as BPD are known to cause imbalance in the muscle strength leading to muscle shortening, weakness and compensatory mechanisms. This muscular imbalance, combined with alterations in lung volume and inspiratory muscular effort can overcome the resistance imposed by the smaller airways 5increasing the pulmonary tension[25], which can cause postural and muscle tone disorders. This phenomenon was observed in our study, since premature infants with BPD showed greater electromyographic activity in the accessory inspiratory muscle. In this line, similar results were found in patients with other respiratory diseases such as asthma, mouth breathers and COPD, in whom increased respiratory effort causing changes in the muscles of the thoracic cage, increasing the muscle activity in EE, large dorsal, PM and TP[26]. Additionally, Ratnovsky et al. reported similar adaptations in the electromyographic activity of the sternocleidomastoid, external intercostal, rectus abdominis and external oblique muscles, in which the increase in respiratory work showed an increase in activity electromyographic image of these muscles, in healthy subjects[27].

There are respiratory and musculoskeletal factors in premature infants which made them vulnerable to respiratory failure. The chest cavity is extremely cartilaginous and with high complacency and during periods of respiratory effort, the chest wall is easily drawn inward, requiring a greater activation of the rib cage stabilizing

TABLE 3. **Electromyographic evaluations during the period of hospitalization in the NICU.**

	1st EMG Ev.			2nd EMG Ev.		
Muscles	BPDG (n = 18)	CG (n = 19)	P	BPDG (n = 18)	CG (n = 19)	P
PM (V)	0.03985_b	0.03475	0.4236	0.034	0.02795_a	0.1424
AS (V)	0.01419_b	0.009717_c	0.0063*	0.01217_b	0.009819_b	0.0979
TP (V)	0.00637	0.00431_a	<0.0001*	0.005395_b	0.004275_b	0.0306*
EE (V)	0.007394	0.006161	0.2545	0.006666_b	0.004252_b	0.0044*
	3rd EMG Ev.			4th EMG Ev.		
Muscles	BPDG (n = 18)	CG (n = 19)	P	BPDG (n = 18)	CG (n = 19)	P
PM (V)	0.03138_b	0.02554_a	0.1886	0.03274_b	0.02346_f	0.1401
AS (V)	0.01424_b	0.009812_b	0.0847	0.01284	0.01262_f	0.9333
TP (V)	0.006391_b	0.004701	0.0064*	0.005971_b	0.004343_f	0.0409*
EE (V)	0.004495_c	0.003937	0.3127	0.005726_f	0.003822_g	0.0331*

NICU: Neonatal Intensive Care Unit; EMG Ev.: Electromyographic Evaluation;
BPDG: Bronchopulmonary Dysplasia Group; CG: Control Group; PM: pectoralis major;
AS: anterior serratus; TP: Trapezius; EE: Erector of the spine;
V: Volts; $_a$ (n = 18), $_b$ (n = 17), $_c$ (n = 16), $_d$ (n = 10), and (n = 09), $_f$ (n = 08), $_g$ (n = 07). * Significance difference P < 0.05.

muscles to maintain the balance and adequate ventilation. These peculiarities are inversely proportional to GA and weight[27-29]. In the present study, the infants with BPD presented lower GA and weight when compared to CG, which may be associated with increasing in the respiratory effort and more activation in inspiratory muscles as compensatory response. Furthermore, the difference between weight, Apgar and GA between groups may be associated with factors such as prematurity, extreme low birth weight and perinatal asphyxia are related to a greater risk of developing BPD[30].

The analysis of the correlations showed a negative association between the muscle tone of TP with positive pressure (used in both IMV and non-invasive) in the second EMG evaluation in BPDG. This inverse relationship can be explained because a positive pressure helps to maintain the functional residual capacity, avoiding pulmonary collapse, giving more stability to the thoracic cavity, and improves the length-tension relation of respiratory muscles, making them more efficient[29-31]. A similar result was reported in a recent study published by Cardoso et al., in which positive pressure reduced the electromyographic activity of the sternocleidomastoid, facilitating ventilation and decreasing the sensation of dyspnea in patients with COPD[31].

There was also a positive association between the muscle tone in TP in the fourth evaluation with the FiO_2 used in the BPDG, hypothesizing that higher O_2 consumption is caused by greater muscle activation. Premature infants with BPD presented altered ventilatory control in the presence of hypoxia, which added to the inefficiency of gas exchange, muscular immaturity and increased respiratory effort, can lead to greater activation of the accessory respiratory muscles[32].

Positive association was also observed between the severity of BPD and the positive pressure used at the time of the second EMG assessment of BPDG. Infants of the BPDG who progressed with more severity required a higher positive pressure. In this line, a positive pressure, despite facilitating the action of TP and possibly reducing the ventilatory effort (as previously observed in the negative association between positive pressure and TP tone at the same time), may also contribute to the pathogenesis of BPD. According to Davidson et al.[33], positive pressure and excess of volume delivered through assisted ventilation can cause lesions in the immature lung with alveolar hyperinflation, leading to the generation of cellular lesions, inflammation and reactive O_2 species. These factors amplify the lesion associated with prenatal inflammation[33], which aggravates the state of the disease.

Understanding such muscular changes that occur in infants with BPD is important to outline the best treatment for these children even during their stay in the ICU, such as physiotherapeutic treatment that, through stretching of the accessory muscles, positioning, joint mobilizations, manual supports, performed to minimizing the use of accessory inspiration and expiration muscles, retraining respiratory work that is overloaded in neonatal pathologies such as BPD, helps to improve breathing patterns, reduce energy expenditure and muscle fatigue[34].

No differences were observed between the groups for PM during hospitalization and AS (after the first evaluation). This result may be explained because the premature infants received daily physical therapy treatment and follow-up with thoracoabdominal rebalancing techniques, including muscle stretching and positioning. These interventions may have contributed to this similarity between tones in the groups in the PM and AS muscles during the NICU admission period and may have reduced the difference observed in the other muscles (TP and EE). In fact, there are authors who argue that adequate positioning promotes postural control, which favors mechanical stimulation, leading to a more synergistic development of musculature, more adequate tonus, broader range of motion and greater active movement[35].

With respect to the behavior of muscles over time, EE in both CG and BPDG presented a reduction in muscle tone, verified by intragroup analysis. These findings agree with the study of Urzêda et al.[36], who assessed the muscular tone in premature infants through passive manipulation of upper and lower limbs and found an initial muscular hypertonia, which disappeared after the interventions. Additionally, the study of Urzêda et al.[36] verified that there was a trend to normalize the muscle tone as the chronological age progresses, which is consistent with the literature, regarding the normal evolution of muscle tone over the months.

There are some limitations in our study; surface electromyography is not totally recommended to measure the muscle activity in specific muscle, when the area is very small as premature infants. This made the bilateral evaluation impossible, which could lead to contamination of the EMG signal (interferences). However, we took some cares to reduce the interferences, such as previous training with EMG equipment, correct positioning of the electrodes, experience to manipulate infants, and shutdown of the incubator at the time of evaluation. Another limitation was not to consider all infants in the same GA, but the study design did not allow it, since this study aimed to follow-up the infants from birth to 36 weeks of GA. Although all infants received physiotherapeutic treatment, hydrotherapy was performed only in infants with BPD, according to the protocol in our unit, which may have influenced the results, since the effects of the therapy, composed of stretching and sensory-motor stimulation techniques, associated with water temperature, could favor decreasing in the muscle tone. Therefore, physiotherapy treatment, may also have been another limitation. Finally, the baseline differences between groups resulting from the selection criteria used to detect BPD may introduce bias into the results.

This study has some strengths. First, this study adds information about the clinical impact of BPD in the activity of respiratory muscles, additionally reported the difference in the ventilatory muscle pattern between infants with and without BPD, and how these differences are maintained over time. Studies in BPD are necessaries since the incidence is augmenting in the last years, since the greater survival of premature infants may increase the risk of comorbidities associated with prematurity. Additionally, the early identification of some disabilities associated to BPD can help in both prevention and treatment in individuals with this disease. Noteworthy, we use EMG to assess the muscle tone, which is an objective,

quantitative and reliable method. On the other hand, most of the studies measured muscle tone through visual observations, and few studies have used EMG in the premature infants so far. Thus, EMG has not been used to assess the muscle tone of preterm infants with BPD, therefore, it denotes the novelty of our study. Early identification of these findings may aid in preventive therapies in BPD and may also support the planning of specific interventions for premature infants with BPD, providing fewer long-term sequelae and better future quality of life for these infants[37].

CONCLUSION

The present study highlights those premature infants with BPD exhibit heightened muscle tone in the trapezius, anterior serratus, and erector spinae muscles —key accessory inspiratory muscles— during their hospitalization in the neonatal intensive care unit. This increased muscle activation is believed to be linked to the elevated requirement for both invasive and non-invasive ventilatory support in this patient group. Given these findings, pulmonary rehabilitation interventions become imperative to reduce the need for ventilatory support and reduce the energetic cost associated with the overactivation of these accessory respiratory muscle groups. By addressing these factors, such interventions aim to prevent potential sequelae in accessory respiratory muscles, thus promoting better long-term respiratory health outcomes in premature infants with BPD.

ETHICAL RESPONSIBILITIES

Protection of people and animals. The procedures followed in this study comply with the basic principles of the Declaration of Helsinki of the World Medical Association, updated in 2013 in Fortaleza (Brazil) and completed with the Taipei declaration of 2016 on ethical considerations on the bases of health data and biobanks.

Confidentiality and informed consent. The authors declare that they are responsible for carrying out the protocols established by their center to evaluate the participating subjects for the purpose of research and scientific dissemination, and guarantee that they have met the requirement of having informed verbally and in writing all the participants who formed part of the study, being in possession of the informed consent signed by the subjects.

Data confidentiality and right to privacy. The authors declare the guarantee of the privacy of the volunteers' data and state that the published manuscript does not violate personal data protection regulations. No names, initials, or medical record numbers (or any type of research data that could identify the participants) are used.

Conflicts of Interest. The authors declare no conflict of interest.

Support source and funding. This study was supported by the Coordination of Improvement of Higher Education Personnel - Brazil (CAPES) - Financing Code 001 and received financial support from the National Council for Scientific and Technological Development (CNPq) [Universal 01/2016 - Track B - Case 402510 / 2016-0].

Author contributions. TRR, DSS, JMF and JCK managed the data collection. TRR and DSS and WSL conceived the paper, methodology, managed the research team and wrote the original draft. LSL, JMF and JCK contributed to the writing of the paper. RAS and VSP conceived the project and the paper; acquired funds; administered the project and supervised its development; and had a leading role in the paper draft. EK and WSL curated the database and carried out the statistical analyses. All authors contributed ideas to the draft of the paper and reviewed and approved its last version. WSL and VSP reviewed the final version of the manuscript.

ACKNOWLEDGMENTS

We would like to thank the professionals from the Hospital, and family members. This work was supported by the Coordination of Improvement of Higher Education Personnel - Brazil (CAPES) - Financing Code 001 and

received financial support from the National Council for Scientific and Technological Development (CNPq) [Universal 01/2016 - Track B - Case 402510 / 2016-0].

BIBLIOGRAPHIC REFERENCES

1. Siffel C, Kistler KD, Lewis JFM, Sarda SP. Global incidence of bronchopulmonary dysplasia among extremely preterm infants: a systematic literature review.J Matern Fetal Neonatal Med. 2021 Jun; 34(11): 1721–31.
2. Dik PHB, Gualdron MN, Galletti MF, Cribioli CM, Mariani GL. Bronchopulmonary dysplasia: incidence and risk factors. Arch Argent Pediatr. 2017 Oct 1; 115(5): 476–82.
3. Jain D, Bancalari E. Bronchopulmonary dysplasia: clinical perspective. Birth Defects Research. 2014 Mar; 100(3): 134–44.
4. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2001; 163(7): 1723–29.
5. Malleske DT, Chorna O, Maitre NL. Pulmonary sequelae and functional limitations in children and adults with bronchopulmonary dysplasia. Pediatr Repiratory Reviews. 2018 Mar; 26: 55–9.
6. Fortuna M, Carraro S, Temporin E, Berardi M, Zanconato S, Salvadori S, et al. Mid-childhood lung function in a cohort of children with "new bronchopulmonary dysplasia". Pediatr Pulmonol. 2016 Oct; 51(10): 1057–64.
7. Bergstrom PU, Halberg J, Thunqvist P, Berggren-Brostrm E, Anderson M, Adenfelt G, et al. Lung function development after preterm birth in relation to severity of Bronchopulmonary dysplasia. BMC Pulmonary Medicine. 2017 Jun 30; 17(1): 97.
8. McGrath-Morrow SA, Collaco JM. Bronchopulmonary dysplasia: what are its links to COPD? Therapeutic Advances in Respiratory Disease. 2019 Jan-Dec; 13: 1753466619892492.
9. Liu K, Yu X, Cui X, Su Y, Sun L, Yang J, Han W. Effects of Proprioceptive Neuromuscular Facilitation Stretching Combined with Aerobic Training on Pulmonary Function in COPD Patients: A Randomized Controlled Trial. Int J Chron Obstruct Pulmon Dis.2021 Apr 13; 16: 969–77.
10. Scavacini AS, Davidson J, Wandalsen GF, Gonçalves DMM, Lanza FC, Goulart AL, et al. Association between thoracic musculoskeletal abnormalities and lung function in preterm infants. Clin Respir J. 2020 Feb; 14(2): 158–64.
11. Tenório RMB. Use of surface electromyography in the qualification of flexor muscle tone in term and preterm newborns. Master thesis. Federal University of Pernambuco, Recife; 2011.
12. Marletti R, Botter A, Trojan A, Merlo E, Minetto MA. Technology and instrumentation for the detection and conditioning of the surface electromyographic signal: state of the art. Clin Biomech. 2009 Feb; 24(2): 122–34.
13. Alves CIS. Validation and Reproducibility of a Screening Scale for Neurological Screening of uncomplicated preterm newborns upon reaching term age. Thesis (doctorate) - Post-Graduation Program in Health Sciences. Federal University of Rio Grande do Norte; 2017.
14. Maekawa K, Ochiai Y. Electromyographic studies on flexor hypertonia of the extremities of newborn infants. Develop Med Child Neurol. 1975 Aug; 17(4): 440–6.
15. Marcus J, Hans SL. Electromyographic assessment of neonatal muscle tone. Psychiatry Res. 1982 Feb; 6(1): 31–40.
16. Diniz KT, Cabral-Filho JE, Miranda RM, Lima GMS, Figueredo NPS, Araújo KFN. Short-time effect of the kangaroo position on electromyographic activity of premature infants: a randomized clinical trial. J Pediatr (Rio J).2020 Nov-Dec; 96(6): 741–7.
17. Miranda RM, Cabral-Filho JE, Diniz KT, Lima GMS, Vasconcelos DA. Electromyographic activity of preterm newborns in the kangaroo position: a cohort study. BMJ Open. 2014 Oct 28; 4(10): e005560.
18. van Leuteren RW, Waal CG, Hutten GJ, Jongh FH,van Kaam AH. Transcutaneous monitoring of diaphragm activity as a measure of work of breathing in preterm infants. Pediatric Pulmonology. 2021 Jun: 56(6): 1593–600.
19. Kraaijenga JV, Waal CG, Hutten GJ, Jongh FH, van Kaam AH. Diaphragmatic activity during weaning from respiratory support in preterm infants. Arch Dis Child Fetal Neonatal Ed. 2017 Jul; 102(4): 307–11.
20. Rosa GJ, Ribeiro T. Monitoring of the tone of the accessory muscles of inspiration through surface electromyography in preterm newborns with and without bronchopulmonary dysplasia: a longitudinal study. 2018. 74p. Master dissertation (Post-Graduate Program in Rehabilitation Sciences - Program in association between UEL - UNOPAR) – Londrina State University, Londrina, 2018
21. Brito ASJ. Perinatal asphyxia. In: Carvalho ABR, Brito ASJ, Ferrari LSL, González MRC. Routines of Neonatology. 2nd ed. London: Oxford University Press. p.121–7.

22. Hermens HJ, Freriks B, Disselhorst-Klug RG. Development of recommendations for SEMG sensors and sensors placement procedures. J Electromyog and Kines. 2000 Oct; 10(5): 361–74.
23. BrazeltonTB. Neonatal behavioral assessment scale. Clinics in Developmental Medicine. 1973; 50: 53–9.
24. Ross SM. Introduction to Probability and Statistics for Engineers and Scientists. 3rd ed. Berkeley, California: Elsevier; 2004.
25. Maccari GM, Pinheiro SG. Bronchopulmonary dysplasia. In: Sarmento GJV (Org.). Respiratory physiotherapy in Pediatrics and Neonatology. Barueri, SP: Manole, 2007. p. 266–81.
26. Garcia KMB, Davidson J, Goulard AL, Santos AMN. Association between preterm birth and thoracic musculoskeletal static alterations in adolescents. Braz J Phys Ther. 2015 Jan-Feb; 19(1): 10–7.
27. Ratnosky A, Zaretsky U, Shiner RJ, Elad D. Integrated approach for in vivo evaluation of respiratory muscles mechanics. J Biomech. 2003 Dec; 36(12): 1771–84.
28. Lima MP. Bases of the thoracoabdominal rebalancing method. In: Sarmento GJV. Resources in cardiorespiratory physiotherapy. São Paulo: Manole, 2012.
29. Okay MC. Neonatal and pediatric physiotherapy. Barueri, SP: Manole, 2012.
30. Costa PFBM, Pulmão RJ. Bronchopulmonary Dysplasia. 2013; 22(3): 37–42.
31. Cardoso DM, Fregonezi GAF, Jost RT, Gass R, Alberton CL, Albuquerque IM, et al. Acute effects of Expiratory Positive Airway Pressure (EPAP) on different levels in ventilation and electrical activity of sternocleidomastoid and parasternal muscles in Chronic Obstructive Pulmonary Disease (COPD) patients: a randomized controlled trial. Braz J Phys Ther. 2016 Nov-Dec; 20(6): 525–34.
32. Bates ML, Pillers DA, Palta M, Farrell ET, Eldridge MW. Ventilatory Control in Infants, Children and Adults with Bronchopulmonary Dysplasia. Respir Physiol Neurobiol. 2013 Nov 1; 189(2): 10.
33. Davidson LM, Berkelhamer SK. Bronchopulmonary Dysplasia: Chronic Lung Disease of Infancy and Long-Term Pulmonary Outcomes. J Clin Med. 2017 Jan 6; 6(1): 4.
34. Roussenq KR, Scalco JC, Rosa GJ, Honório GJS, Schivinski CIS. Rebalancing thoracoabdominal movements in preterm infants: effects on cardiorespiratory parameters, in behavior, in pain and in the respiratory effort. Acta Fisiatr. 2013; 20(3): 118–23.
35. Calazans PPF, Amaral SP, Pinheiro HA, Gardenghi G. Analysis of reflexes in premature infants undergoing functional positioning in a Neonatal Intensive Care. Con Scientiae Saúde. 2015; 14(1): 147–52.
36. Urzêda RN, Oliveira TG, Campos AM, Formiga CKMR. Reflexes, reactions and muscle tone of preterm infants in an early intervention program. Rev Neurosciences. 2009; 17(4): 319–25.
37. Gou X, Yang L, Pan L, Xiao D. Association between bronchopulmonary dysplasia and cerebral palsy in children: a meta-analysis. BMJ Open. 2018 Sep 19; 8(9): e020735.