Influence of the selective insufflation technique on cerebral blood flow in preterm infants

Influência da técnica de insuflação seletiva no fluxo sanguíneo cerebral de prematuros

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Abstract

Introduction: The intervention of respiratory physiotherapy in neonatal units is in continuous development, having its own care characteristics related to the weight and gestational age of the newborn, respecting the immaturity of the organs and systems and the diseases of this patient. Through techniques, the objective is to optimize the respiratory function, assisting in the clearance of secretions, and the restoration of lung volumes. **Objective:** To verify if the respiratory physiotherapy technique of selective insufflation alters the cerebral blood flow in premature infants under 34 weeks of gestational age. **Methods:** This is an uncontrolled clinical trial, conducted in a Neonatal Intensive Care Unit of a level III hospital, between January 2019 and March 2020, with participation of premature newborns under 34 weeks of gestational age. All were submitted to transfontanellar Doppler ultrasonography to assess cerebral blood flow measurements, mainly the resistance index, before and after the application of the selective insufflation respiratory physiotherapy technique. **Results:** Sixty-two newborns were included, with a mean gestational age of 29.3 ± 2.2 weeks and birth weight of 1,259 ± 388 grams. The resistance index did not change significantly (RI before: 0.55 ± 0.07; after: 0.54 ± 0.07; p = 0.06) before and after the intervention and no studied variables such as, gender, gestational age, weight, Apgar score or SNAPPE II score had an influence on cerebral blood flow measurements. **Conclusion:** The selective insufflation technique did not alter cerebral blood flow in premature newborn infants under 34 weeks gestational age.

Keywords: Cerebrovascular circulation. Hospital physical therapy department. Infant premature. Neonatal intensive care units.

Resumo

Introdução: *A intervenção da fisioterapia respiratória nas unidades neonatais está em contínuo desenvolvimento, tendo características próprias de atendimento relacionadas ao peso e à idade gestacional do recém-nascido, respeitando a imaturidade dos órgãos e sistemas e as doenças desse paciente.* ***Objetivo:*** *Verificar se a técnica de fisioterapia respiratória de insuflação seletiva altera o fluxo sanguíneo cerebral de prematuros menores de 34 semanas de idade gestacional.* ***Métodos:*** *Trata-se de um ensaio clínico não controlado, realizado em uma Unidade de Terapia Intensiva Neonatal de um hospital nível III, entre janeiro de 2019 e março de 2020, com a participação de recém-nascidos prematuros menores de 34 semanas de idade gestacional. Todos foram submetidos ao exame de ultrassonografia transfontanela com Doppler para avaliar as medidas de fluxo sanguíneo cerebral, principalmente o índice de resistência, antes e depois da aplicação da técnica de fisioterapia respiratória de insuflação seletiva.* ***Resultados:*** *Sessenta e dois recém-nascidos foram incluídos, com média de idade gestacional de 29,3 ± 2,2 semanas e peso de nascimento de 1259 ± 388 gramas. O índice de resistência não se modificou de forma significativa antes e depois da intervenção (IR antes: 0,55 ± 0,07; depois: 0,54 ± 0,07; p = 0,06) e nenhuma variável estudada, como sexo, idade gestacional, peso, escore de Apgar ou escore SNAPPE II, teve influência nas medidas de fluxo sanguíneo cerebral.* ***Conclusão:*** *A técnica de insuflação seletiva não alterou o fluxo sanguíneo cerebral de recém-nascidos prematuros menores de 34 semanas de idade gestacional.*

Palavras-chave: *Circulação cerebrovascular. Serviço hospitalar de fisioterapia. Recém-nascido prematuro. Unidades de terapia intensiva neonatal.*

Introduction

The intervention of respiratory physiotherapy in neonatal units is in continuous development, having its own care characteristics related to the weight and gestational age of the newborn, respecting the immaturity of the organs and systems and the diseases of this patient.[1] Through techniques, the objective is to optimize the respiratory function, assisting in the clearance of secretions, and the restoration of lung volumes.[1,2]

The care must be performed by a specialized professional, who knows how to determine the need and the moment to intervene, with a well elaborated program, respecting the physiological and anatomical particularities of the newborn baby. The use of inappropriate techniques may cause instability and expose the newborn to adverse effects.[1-3]

The developing premature newborn brain is extremely vulnerable. One of the aims of all neonatal care should be the prevention of brain damage.[4] Newborns with birth weights less than 1,500 grams are particularly susceptible to brain injury, since autoregulation of cerebral blood flow (CBF) is not yet adequately established especially during the first five days after birth. Thus, it is essential to minimize blood pressure fluctuations by reducing handling, discomfort, and stress. The more premature the newborn, the more unstable and higher the risk of brain damage.[5]

Besides brain immaturity, premature birth also interferes in pulmonary development and the occurrence of the Respiratory Distress Syndrome is frequently observed, caused mainly by insufficiency in the production of surfactant and pulmonary immaturity, generating the need for ventilatory support with positive pressure in an invasive or non-invasive way and the offer of supplementary oxygen. Lung disease causes increased production of bronchial secretion and increases the occurrence of collapse of lung areas, generating atelectasis.[6,7]

The respiratory physiotherapy technique of selective insufflation is indicated to re-expand collapsed areas, restoring lung volumes. It consists of gently applying manual chest compression to one of the newborn's hemithoraxes so that the expansion of the contralateral hemithorax is favored. However, its influence on the CBF of preterm infants is not documented in the literature.[8-10]

In this context, the objective of the present study was to verify whether the selective insufflation technique alters the CBF of premature newborns assessed by means of transfontanellar Doppler ultrasonography.

Methods

This is an uncontrolled, before-and-after clinical trial conducted in a level III neonatal intensive care unit (ICU) between January 2019 and March 2020. The study was approved by the Ethics Committee of the Clinics

Hospital Complex of Universidade Federal do Paraná, under opinion number 2,848,638, and registered in the Brazilian Clinical Trials Register database (RBR-56swpv), available to the public.

Newborns under 34 weeks of gestational age were included in the study, whose guardians accepted the invitation and signed the informed consent form. Newborns with congenital malformations, grade III and IV peri intraventricular hemorrhage, contraindications for respiratory physiotherapy with application of chest techniques (pulmonary hemorrhage, severe pulmonary hypertension, undrained pneumothorax, severe thrombocytopenia, recent postoperative period or presence of chest tube) and those transferred to another service before evaluation was possible, were excluded.

At the time of the assessment, the newborns were clinically stable, breathing in room air or with oxygen supplementation, invasive or non-invasive ventilation, whose parameters and modalities were recorded. When agitated or crying, they were firstly comforted and, if necessary, non-nutritive sucking with gloved finger was used. When necessary, bronchial hygiene and aspiration of pulmonary secretions were performed before the evaluation, and the newborn remained unmanipulated for at least thirty minutes after this procedure.

The handling of premature babies occurred one hour before feeding, and in cases of fasting, it was performed before nursing care, always respecting the minimum handling protocol of the ICU. When necessary, the inspired oxygen fraction was increased up to 20% of the baseline value during the procedure, other parameters of mechanical ventilation were not altered during the intervention.

During all the handling, the newborns remained in their incubators, accommodated in their "nests", made with linens, whose use is standardized by the ICU, for comfort and to facilitate adequate posture. The temperature of the newborn was previously checked by the nursing professional responsible for care and the maximum handling time was 20 minutes.

With the newborn in dorsal decubitus, head in midline, the first Doppler ultrasound examination was performed by a single specialist physician, the findings were noted on the evaluation form. Then, the application of the respiratory physiotherapy technique was started and soon afterwards the Doppler ultrasound was repeated. The final results were also recorded, as well as the vital signs, evaluation by the pain scale and any alteration that occurred during the procedure.

The technique evaluated in the study was selective insufflation, which consists of gently and manually applying chest compression at the end of expiration on an entire hemithorax, with the newborn in dorsal decubitus and head centered.[9] The release phase was always performed slowly. Chest compression was maintained for three timed minutes on the left hemithorax in all participants for standardization purposes, taking into consideration the newborn's clinical condition, ventilatory parameters, chest expansion and pulmonary auscultation at the time of evaluation. Those who were under invasive mechanical ventilation were evaluated only after radiological imaging that ensured the correct position of the cannula, avoiding handling newborns with atelectasis to the left due to malpositioning of the cannula. The technique was always applied by the same physiotherapist.

CBF was evaluated by means of measurements obtained by transfontanellar Doppler ultrasound. The examination was performed during the study period following the routines of the service, at the bedside, by a pediatric neurologist physician who has specific training in cerebral ultrasonography and expertise in the area. The artery chosen for study was the pericallosal, a branch of the anterior cerebral artery, located adjacent to the genu of the corpus callosum, and the following parameters were assessed: RI (resistance index = SFV-DFV/SFV); systolic flow velocity (SFV) and diastolic flow velocity (DFV). The pericallosal artery was the first choice, but if this was not possible, due to the premature babies' characteristics, adjacent branches were used for measurement. The evaluation was made of at least five sequential stable waveforms for analysis. The Sono Site device, model M-Turbo®, with a 5 MHz transducer was used.

During the whole procedure, vital parameters monitoring (heart rate; respiratory rate and peripheral oxygen saturation) was strictly carried out. The criteria for interruption were as follows: if the newborn presented signs of intolerance, such as bradycardia or drop in oxygen saturation to 20% of the initial value without immediate return with increased inspired fraction of oxygen, or signs of pain and stress without immediate consolation, pain was assessed using the Neonatal Infant Pain Scale (NIPS).

Data collection and analysis

The data collected were obtained from the newborn's medical record and entered into a secure database. The data included: sex, birth weight, classification of the degree of prematurity in relation to gestational age (extreme, very premature, moderate) and weight (extreme low, very low, low), Apgar score, Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE II), use of antenatal corticoid and exogenous surfactant. Clinical results during hospitalization or at the time of collection such as invasive or non-invasive mechanical ventilation, use of supplementary oxygen, heart rate, respiratory rate, peripheral oxygen saturation, and presence of pain were also collected.

Descriptive statistics were performed, the measures of central tendency and dispersion are expressed as means and standard deviation for the symmetrical continuous variables and as medians, minimum and maximum for the asymmetrical ones. Categorical variables are expressed in absolute and relative frequency. For the analysis of continuous variables of dependent samples and for independent groups the Student's t test was performed. For analysis of more than two independent groups one-way Anova and the Duncan post hoc test was used. Categorical variables were analyzed considering the chi-square test. Statistical analysis software Statistic (Statsoft®) was used. The sample size calculation was performed using the statistical program G* Power 3.1®, considering a type I error of 5% and type II error of 10%, a sample size of 62 newborns was determined (two-tailed test).

Results

A total of 136 newborns were admitted to the ICU during the study period, of which 78 met the inclusion criteria and were recruited. Among those eligible for evaluation there were 16 sample losses (Figure 1).

The sample consisted of 62 premature newborns, 41 (66.1%) males, with a mean gestational age of 29.3 ± 2.2 weeks and birth weight of 1,259.0 ± 388.0 grams. Regarding the use of antenatal corticoids, 55 (88.7%) mothers used them. At the fifth minute of life, 15 (24.2%) presented an Apgar score between 4 and 7 points, while 47 (75.8%) scored between 8 and 10. Of all, only 20 (32.3%) required exogenous surfactant.

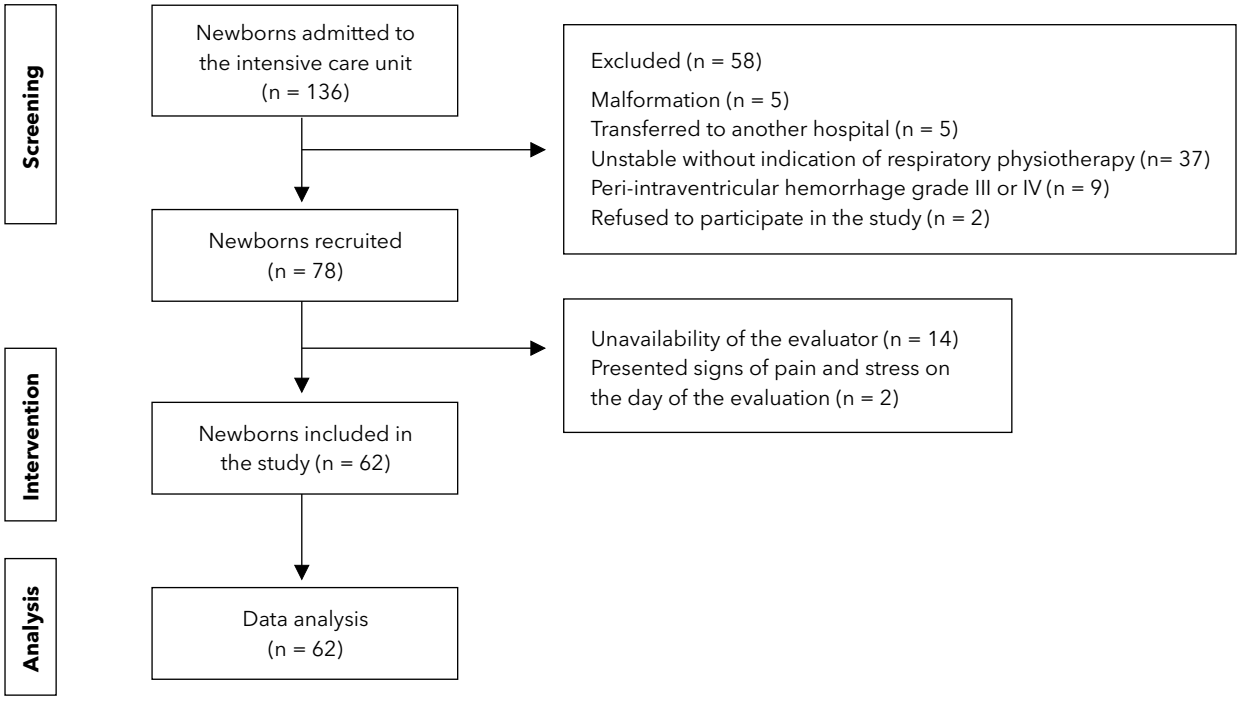

Figure 1 - Flow chart for data collection.

The SNAPPE II Severity Score ranged from 0 to 92 points, with nine (14.5%) scoring 39 or more and 50 patients (80.6%) scoring less. This score could not be assessed in three patients (4.8%), due to the absence of necessary information in the medical record.

The 62 newborns underwent a single assessment, performed on average at 7.7 ± 3.2 days of life. The mean weight at the time of evaluation was 1,206.0 ± 318.0 grams. Other information regarding ventilatory support is described in Table 1.

The CBF measurements studied are shown in Table 2. It is observed that the RI and the DFV were not significantly altered after the selective insufflation technique, but there were significant alterations in the SVF measurements. Table 3 shows the analysis performed between the absolute measurements of CBF before and after the application of the technique and, the weight, gestational age and ventilatory support on the day of the evaluation.

Table 1 - Clinical characteristics of the study participants (n = 62)

Characteristics	n (%)
Ventilatory support	
Ambient air	26 (41.9)
Using nasal oxygen catheter	4 (6.5)
In Non-invasive ventilation	20 (32.3)
In invasive mechanical ventilation	12 (19.4)
Fraction of inspired oxygen	
Greater than 40%	5 (8.1)
Less than 40%	57 (91.9)

Note: Data demonstrated in absolute and relative frequency.

Table 2 - Cerebral blood flow (CBF) measurements before and after application of the selective insufflation technique (n = 62)

CBF (cm/s)	Before	After	p*
RI	0.55 ± 0.07	0.54 ± 0.07	0.06
SFV	26.70 ± 5.67	26.1 ± 5.57	0.01
DFV	11.8 ± 3.24	11.7 ± 2.91	0.82

Note: Data shown as mean and standard deviation. RI = resistance index; SFV = systolic flow velocity; DFV = diastolic flow velocity. *t Student for dependent sample.

Table 3 - Distribution of the CBF measurements before and after the action of the respiratory physiotherapy technique according to the study (n = 62)

Variable	RI before	p*	RI after	p*
Weight				
Extreme low	0.55		0.55	
Very low	0.55	0.96	0.53	0.70
Low	0.55		0.53	
Post-menstrual GA				
Extreme	0.61		0.58	
Very premature	0.55	0.34	0.53	0.69
Moderate	0.54		0.53	
Ventilatory support				
Ambient air	0.54		0.52	
Nasal O_2 catheter	0.56	0.12	0.54	0.05
NIV	0.53		0.52	
IMV	0.59		0.59	

Note: Data shown as mean. Weight and gestational age corrected according to their ratings on the day of the evaluation. CBF = cerebral blood flow; RI = resistance index (cm/s); GA = gestational age; O_2 = oxygen; NIV = non-invasive ventilation; IMV = invasive mechanical ventilation. *Anova one-way; post hoc Duncan's.

At the initial ultrasound, 10 (16.1%) preterm infants had grade I or II PIVH and 52 (83.9%) presented normal exams. It was observed that the values of initial and final SVF and DFV were higher in the group with PIVH, as can be seen in Table 4.

The median length of hospital stay was 43 days, with a minimum of 13 and a maximum of 111 days. Of the 62 preterm infants monitored, 60 (96.8%) were discharged from hospital and 2 (3.2%) died during hospitalization, one due to complications in a surgical procedure (54 days of life) and the other due to sepsis (25 days of life).

Discussion

This study has shown that the technique of respiratory physiotherapy of selective insufflation did not significantly alter the CBF in newborns even in those with PIVH grade I and II, which corresponded to 16.1% of the sample. These findings are relevant considering that very premature newborns, 29.3 ± 2.2 weeks of gestational age and very low birth weight, 1,259.0 ± 388.0 grams were studied.

Table 4 - Distribution of cerebral blood flow measures and the study variable (n = 62) before and after evaluation

	PIVH grade I or II			Sex			Apgar score at 5 minutes			FiO_2		
	Yes (n = 52)	Não (n = 10)	p*	M (n = 41)	F (n = 21)	p*	4 - 7 (n = 15)	8 -10 (n = 47)	p*	< 40% (n = 56)	≥ 40% (n = 6)	p*
RI before	0.56 ± 0.07	0.51 ± 0.07	0.07	0.54 ± 0.06	0.57 ± 0.08	0.15	0.54 ± 0.08	0.55 ± 0.07	0.83	0.54 ± 0.06	0.64 ± 0.09	0.002
RI after	0.54 ± 0.08	0.50 ± 0.06	0.14	0.52 ± 0.06	0.56 ± 0.09	0.05	0.54 ± 0.07	0.54 ± 0.08	0.99	0.53 ± 0.07	0.63 ± 0.09	0.003
SFV before	26.13 ± 5.37	30.10 ± 6.29	0.04	26.30 ± 5.40	27.60 ± 6.10	0.38	26.80 ± 7.02	26.70 ± 5.25	0.94	26.50 ± 5.77	29.10 ± 4.07	0.330
SFV after	25.49 ± 5.18	29.34 ± 6.64	0.04	25.70 ± 5.50	26.70 ± 5.60	0.51	26.00 ± 6.99	26.10 ± 5.12	0.98	25.90 ± 5.66	27.50 ± 4.60	0.560
DFV before	11.26 ± 2.40	14.76 ± 5.19	<0.01	11.90 ± 3.31	11.60 ± 3.16	0.75	12.00 ± 4.84	11.70 ± 2.6	0.72	11.90 ± 3.30	9.92 ± 1.65	0.170
DFV after	11.27 ± 2.54	14.37 ± 3.41	<0.01	12.00 ± 3.04	11.20 ± 2.64	0.29	11.60 ± 3.14	11.80 ± 2.87	0.87	11.90 ± 2.92	9.70 ± 2.10	0.090

Note: Data demonstrated as mean and standard deviation. PIVH = peri-intraventricular hemorrhage; M = male; F = female; FiO_2 = fraction of inspired oxygen; RI = resistance index; SFV = systolic flow velocity; DFV = diastolic flow velocity. *t Student, independent groups.

The assessment of CBF in the neonatal period is still a challenge. Although ultrasound is an easily accessible device to assess cerebral circulation in the premature at the bedside, measurement of parameters is difficult in small-caliber vessels.[11] Absolute velocity measurements such as SFV and DFV are difficult to compare because they depend on the insonation angle. On the other hand, the RI value is not affected by changes in this angle and is reproducible, with high inter-observer reliability.[11,12] Thus, the RI was considered a reliable parameter to evaluate the safety of the respiratory physiotherapy technique and no difference was observed in this index when comparing the moments before and after the intervention (p = 0.06), nor regarding the values of DFV (p = 0.82). For the SFV values, there was a statistically significant difference, with a very slight reduction after the application of the technique, when compared to the previous moment (p = 0.01), but these findings may be related to the limitations of the technique mentioned, without clinical significance.

Similarly, in their research Bassani et al.[13] aevaluated the influence of the technique of increased expiratory flow on CBF in 40 premature infants under 34 weeks of gestational age, with a mean weight of 1,658 grams, who breathed with ambient air or with the aid of nasal oxygen catheter, by means of transfontanellar Doppler ultrasound. The measurements of CBF were evaluated before, during and after physiotherapy with the technique of increased expiratory flow, as well as the vital parameters of the newborns. No significant changes were observed in the measurements of CBF or vital data with the application of the technique and the authors concluded that respiratory physiotherapy did not bring about changes in the CBF of the studied newborns.[13]

It is known that the ventilatory strategy in the neonate requiring support has consequences on the pulmonary and cardiovascular system and the immature brain. The alteration of the pulmonary venous return and consequently of the left ventricular output, results in fluctuation of the CBF.[14] Studies show that mechanically ventilated newborns have a lower CBF than those in spontaneous breathing.[15,16] In the present study, even in newborns that received positive pressure (51.7% of the sample), the selective insufflation technique proved to be safe, as there were no changes in the RI when compared to the newborn under spontaneous ventilation.

Assis and Machado[17] examined 100 newborns with gestational age between 28 and 36 weeks and birth weight from 720 to 2,530 grams divided into two groups, one with normal ultrasound (45) and the other with PIVH (55). The RI was measured and, when comparing the 2 groups, they concluded that the RI values were always higher in newborns without hemorrhage than in newborns with hemorrhage. In the present study there was no statistically significant difference in the RI between the groups with and without hemorrhage, although the group with PIVH was smaller (10 newborns), changes were found only in the absolute values of SFV (p = 0.04) and DFV (p < 0.01).

Ecury-Goossen et al.[12] analyzed the RI in several cerebral arteries in a cohort of premature newborns under 29 weeks gestational age, measuring from the first day of life and then weekly until hospital discharge or death and found no significant relation between RI and SNAPPE II score, gestational age or gender. This relationship was also not found in the present study.

Alterations in cerebral perfusion and oxygenation have been implicated in the pathogenesis of brain injury, but without reliable quantitative brain monitoring at the bedside, the identification of newborns at risk and the development of strategies to avoid it are still incipient initiatives.[18] Traditionally, the most widely used technique for this assessment is Doppler ultrasound, which is not always widely available. Another non-invasive way of continuously assessing CBF is the measurement of regional cerebral oxygen saturation by Near Infrared Spectroscopy (NIRS), which measures regional cerebral oxygen saturation and can provide an early warning of low CBF and cerebral oxygenation levels, potentially aiding in the prevention of intraventricular haemorrhage or periventricular leukomalacia in neonates. It is however a technology with limited availability for use in neonatal ICUs.[19]

A study using NIRS aimed to examine the circulatory changes experienced by the brain during routine events of critical newborn care, including 82 patients with birth weight less than 1,500 grams. The effect of clinical factors such as chorioamnionitis, birth weight, SNAPPE II score and cranial ultrasound abnormalities on systemic and cerebral hemodynamic changes was verified. The most significant cerebral hemodynamic alterations were associated in those newborns who presented early parenchymal ultrasonographic abnormalities.[20] These results emphasize the need for a more attentive look at the newborns presenting with brain injury already detected or at potential risk. Other authors in their studies with respiratory physiotherapy techniques applied in the neonatal public, found no evidence of a relationship between these techniques and brain injury.[21,22]

Preterm infants have immature hemodynamic regulation and the relationship between CBF velocity and brain damage has been confirmed in several studies.[23-25] Several clinical events, some related to the care of the premature baby, may generate hemodynamic disturbances that contribute to cerebral blood flow velocity fluctuations. With the results of the present study, respiratory physiotherapy with the selective insufflation technique does not seem to be one of them. However, the neonatal thoracic manipulation should not be seen as risk-free and requires a high level of knowledge, as well as an individualized look at each newborn attended to.

Many studies that relate physiotherapy to brain injuries are old and do not match the care provided nowadays.[26] With the evolution of care, minimal handling, better heating of the gases offered, correct positioning of the premature, improvement of assessment and appropriate choice of techniques used such complications need to be reassessed.

Despite important results, the present study has some limitations. A larger sample size was expected, however the onset of the COVID-19 pandemic in March 2020 changed the collections and examination routines in the Neonatal ICU. It is also noteworthy that it was not possible to "blind" the physician responsible for performing the ultrasound, in relation to the moment before and after the application of the chest physiotherapy technique, which could influence the interpretation of results. However, to minimize this possible bias, he did not have access to the data collected systematically and was not involved in their analysis and statistical treatment.

Another possible limitation consists in the fact that CBF measurements were evaluated only once in each patient, respecting the protocol of the ICU in which brain ultrasounds were performed weekly and not exposing newborns to additional examinations only for research purposes. Serial measurements could eventually bring additional information and allow the study of changes over time.

It is also noteworthy that, although Doppler ultrasound is a non-invasive and easily accessible device, measurement of the parameters is difficult in small-caliber vessels. It was not possible to always measure the hemodynamic values of the same cerebral artery proposed, the pericardial artery, in some cases it was performed of adjacent arteries, mainly in extreme premature babies.

Finally, it is important to mention that blood pressure was not measured in the present research, despite being an important physiological variable in the evaluation of variations in CBF. This occurred due to the study design and inclusion criteria proposed, since blood pressure measurement in the ICU where the research was conducted occurs predominantly by oscillometry. Thus, it was assessed that it would not be possible to

obtain reliable results of blood pressure during handling for ultrasound and physiotherapy, as it is recommended that such measurements be performed with the patient at rest.[27] The strategy considered the gold standard for blood pressure measurement would be the invasive form, which would also allow the evaluation of its alterations during the application of the physiotherapy technique. However, not all newborns were indicated for the invasive device, reserved, due to the risks, for unstable or severely ill newborns. Nevertheless, even though blood pressure measurement was not available in the patients studied, it is reasonable to assume that there were no major changes since only stable newborns were included in the study.

Conclusion

The study provided knowledge on how the CBF of premature newborns behaves after the application of the selective insufflation technique of respiratory physiotherapy and how it interferes on the physiological parameters. It proved to be a procedure without deleterious repercussions in the population studied, that is, a safe technique to be used in premature newborns.

Studies evaluating the safety and effects of respiratory physiotherapy techniques in the neonatal and premature population are necessary, there are few clinical trials addressing the subject.

Authors´contributions

EOG, MGA, and RPGVCS were responsible for the study conception, and SAA, SRV, and RPGVCS for its design. Data analysis and interpretation were done by EOG, MGA, SRV, and RPGVCS, and manuscript writing by EOG. All authors reviewed the manuscript and approved the final version.

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