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Systematic review

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Bronchic hygiene techniques in newborns and infants in the intensive care unit: systematic review of clinical trials

Técnicas de higiene brônquica em recém-nascidos e lactentes na unidade de terapia intensiva: revisão sistemática de ensaios clínicos

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RESUMO | INTRODUÇÃO: A fisioterapia respiratória tem obtido um importante espaço e reconhecimento ao possibilitar resultados de grande eficácia no tratamento intensivo do recém-nascido (RN) e do lactente. Um dos importantes objetos de trabalho da fisioterapia na Unidade de Terapia Intensiva (UTI) neonatal e pediátrica são as técnicas de higiene brônquica rotineiramente utilizadas, as quais apresentam grande variabilidade. **OBJETIVO:** Verificar as evidências científicas a respeito dos possíveis efeitos benéficos ou adversos, indicações e contraindicações das técnicas de higiene brônquica mais utilizadas no RN e no lactente na UTI. **MATERIAIS E MÉTODOS:** Trata-se de uma revisão sistemática, utilizando ensaios clínicos, sem delimitação temporal, baseada no protocolo PRISMA. Foram utilizadas as seguintes bases de dados: PubMed, LILACS, SciELO, PEDro e ScienceDirect. **RESULTADOS:** Foram identificados um total de 154 artigos, apenas 10 atenderam aos critérios de inclusão. Destes 5 (50%) associam tapotagem/percussão torácica, drenagem postural, aspiração de vias aéreas superiores e/ou traqueal e vibração e/ou vibrocompressão torácica manual; 1 (10%) associa drenagem, vibração e percussão; 1 (10%) associa vibrocompressão e aspiração nasotraqueal; 1 (10%) associa percussão e vibração torácica; 1 (10%) estudo utiliza a aspiração traqueal e 1 (10%) utiliza a vibrocompressão torácica manual. **CONCLUSÃO:** A maioria dos estudos encontrados não relataram contraindicações relevantes para impedir o uso de técnicas de higiene brônquica na UTI neonatal e pediátrica, entretanto, alguns resultados foram controversos quanto a sua correta e eficaz indicação.

PALAVRAS-CHAVE: Fisioterapia. Lactente. Recém-nascido. Unidades de Terapia Intensiva.

ABSTRACT | INTRODUCTION: Respiratory physiotherapy has been an important space and is capable of great efforts in the treatment of the newborn (NB) and the infant. The main work items of neonatal and pediatric intensive care unit (ICU) are the routinely used bronchial hygiene techniques, such as those with great variability. **OBJECTIVE:** To verify the scientific evidences regarding the possible beneficial or adverse effects, indications and contraindications of the bronchic hygiene techniques most used in the NB and the infant in the ICU. **MATERIALS AND METHODS:** It is a systematic review, using clinical trials, without temporal delimitation, based on the PRISMA protocol. The following databases were used: PubMed, LILACS, SciELO, PEDro and ScienceDirect. **RESULTS:** A total of 154 articles were identified, only 10 met the inclusion criteria. These 5 (50%) associate tapping/thoracic percussion, postural drainage, aspiration of upper airways and/or tracheal and vibration and/or manual thoracic vibrocompression; 1 (10%) associates drainage, vibration and percussion; 1 (10%) associated vibrocompression and nasotracheal aspiration; 1 (10%) associates percussion and thoracic vibration; 1 (10%) study uses tracheal aspiration and 1 (10%) uses manual thoracic vibrocompression. **CONCLUSION:** Most studies found no relevant reported contraindications to prevent the use of bronchic hygiene techniques in the neonatal and pediatric ICU, however, some results were controversial as its correct and effective statement.

KEYWORDS: Physical therapy specialty. Infant. Newborn infant. Intensive Care Units.

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Introduction

The constant scientific and technological development in the area of perinatal and neonatal care in the last decades has been determinant for the increase of the survival of newborns (RN) with birth weight and gestational age lower and lower[1]. These factors are determinant for the increase of the hospitalization period of these patients, especially of preterm newborns (PTNB)[2]. In addition, pulmonary immaturity and consequent respiratory complications that lead the newborn to remain for prolonged periods under ventilatory support and/or oxygen therapy are particularly noteworthy, making them susceptible to the complications of mechanical ventilation[2,3].

Often infants are affected by respiratory infections, such as acute viral bronchiolitis (AVB), which is responsible for high morbidity and mortality among all children in the world. Between 1% and 3% of infants who develop this infection are hospitalized and up to 15% need to be admitted to an intensive care unit (ICU)[4].

Respiratory physiotherapy has obtained an important space and recognition to contribute to the reduction of the factors presented above, resulting in the possible efficacy of the intensive treatment of the newborn and the infant. It has as one of the important objects of work in the neonatal and pediatric ICU the techniques of bronchial hygiene and, among the most discussed, are manual thoracic vibration, manual thoracic vibrocompression, tapping or thoracic percussion, defined as the application of a combination of forces in the thoracoabdominal region to displace and / or remove secretions from the airways, in addition to commonly used aspiration and postural drainage[5,6,7].

Although studies on bronchial hygiene techniques in newborns and infants, the results are controversial due to the variety of techniques used, as well as the lack of standardization of the correct and safer application. contraindications and possible adverse effects, which causes the need for a greater precision in the use of the techniques for a more careful choice of the physiotherapeutic procedures, which can be evaluated and performed individually according to each patient[3,4,8].

Thus, the purpose of the present study is to verify the scientific evidence regarding the possible beneficial or adverse effects, indications and contraindications of the bronchial hygiene techniques most used in newborn and infants in the intensive care unit.

Materials e methods

This is a systematic review study based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[9]. The following databases were searched for identification of the articles: PubMed, LILACS, SciELO, PEDro and ScienceDirect, without temporal delimitation, in order to cover all the articles produced within the subject matter. Multiple combinations of the following descriptors were used in portuguese, english and spanish: “Newborn”, “Infant”, “Intensive Care Units” e “Physical Therapy Specialty”, using the boolean operators “AND” and “OR”. In the ScienceDirect database, the descriptors cited above were used in english only. In the PEDro database only the english descriptor “Intensive Care Units” was used.

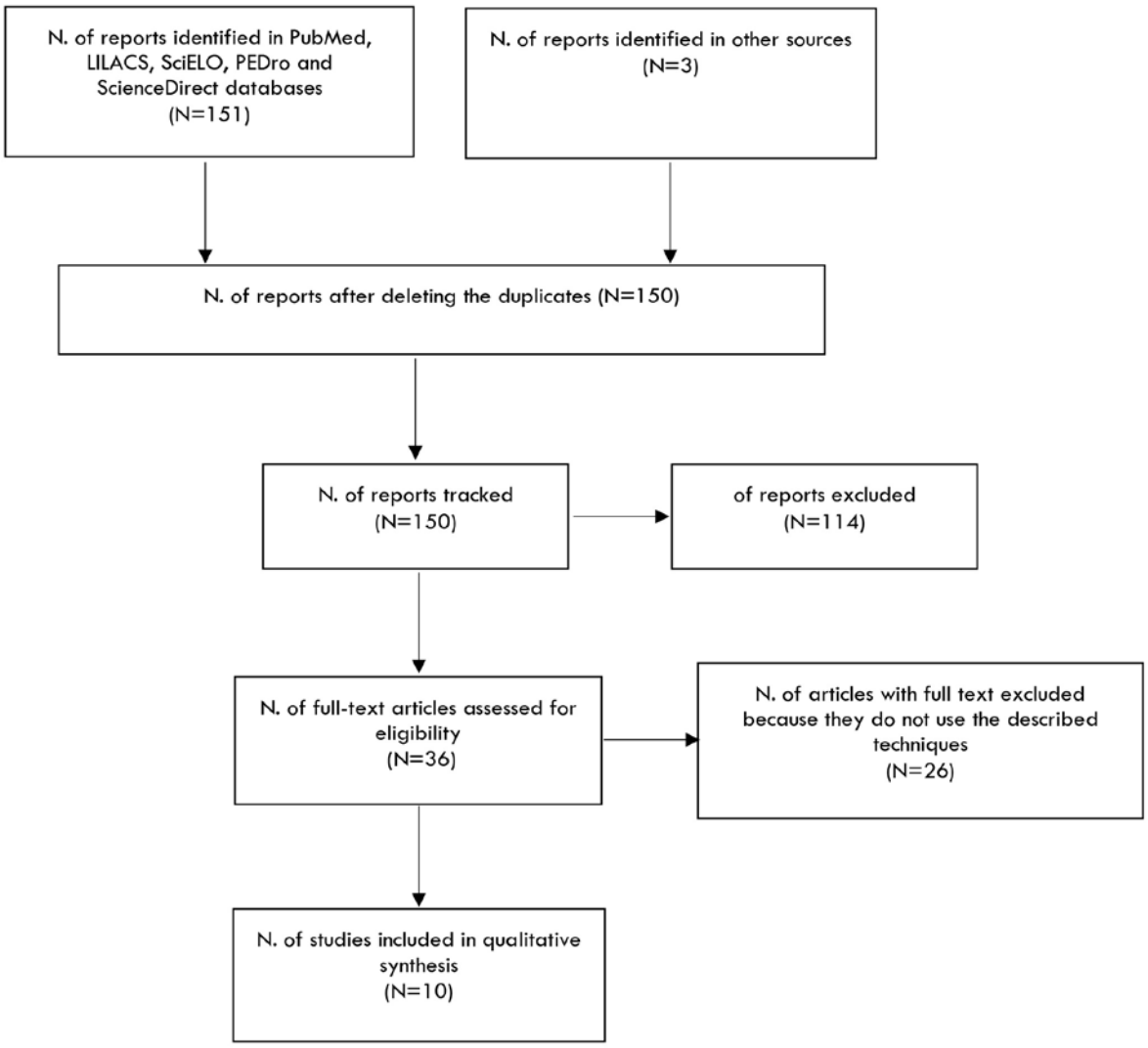
During the selection process, the first step consisted in the process of identifying the studies by their title, behind, after reading the summaries of the identified studies, the analysis of the inclusion criteria was applied, these being: clinical trials in portuguese, english and spanish, performed with newborns or infants, and these were in the ICU, having been applied to respiratory physiotherapy encompassing one or more of a bronchial hygiene technique. If the abstract is sufficient for the article to be included according to the described criteria, the full version was obtained for confirmation and inclusion of the study. However, if this is not enough, the article will be read in its entirety to define its eligibility. Exclusion criteria were articles that were not using at least one bronchial hygiene technique, which included children and did not have a clearly described protocol, as well as case reports and reviews. For the data collection to be effective, a consensus meeting was held between the two researchers involved to analyze the results found regarding the presence of agreement or divergence of these. There was no divergence between the results identified in the searches.

From this, we started the collection in the articles selected to define which characteristics of the studies would be analyzed. The information extracted from the selected articles was organized into a systematic review chart containing the following information: first author and year, type of study, sample, variables and evaluation, intervention and results. To evaluate the methodological quality of the randomized clinical trials, the PEDro scale was used, which is a tool that analyzes the quality of randomized clinical trials and also evaluates its statistical description, that is, whether the study contains minimum statistical information so that the results can be interpreted[10].

Results

According to the initial search, carried out in the databases PubMed, LILACS, SciELO, PEDro and ScienceDirect, in September 2017, a total of 154 articles were identified. After the preliminary reading of the titles and abstracts, 114 articles were excluded, of which 4 were duplicates. After reading the articles in full, 26 were excluded because they did not use the bronchial hygiene techniques described in this study. At the end, 10 studies were included for this systematic review according to the PRISMA protocol[9], Figure 1.

Figure 1. Flowchart of search and selection of studies the studies of Bronchial Hygiene in Newborn and Infants, 2018.



The articles included are clinical trials published between 2003 and 2013, that is, from the year 2013, there are no clinical trial studies that address this topic. Chart 1 presents the sample characterization, variables, intervention and main results of each included study.

Of the 10 articles selected, 5 (50%) associate tapping/thoracic percussion, postural drainage, aspiration of upper airways and/or tracheal and vibration and/or manual thoracic vibrocompression; 1 (10%) associates drainage, vibration and percussion; 1 (10%) associated vibrocompression and nasotracheal aspiration; 1 (10%) associates percussion and thoracic vibration; 1 (10%) study uses tracheal aspiration and 1 (10%) uses manual thoracic vibrocompression.

Regarding the methodological quality of the included randomized clinical trials, relatively all the studies were considered of good quality, since they reached a score equal to or higher than 7 on the PEDro scale10, Index 1.

Index 1. Evaluation of the methodological quality the studies of Bronchial Hygiene in Newborn and Infants according to the PEDro scale, 2018.

AUTHOR/ YEAR	1	2	3	4	5	6	7	8	9	10	11	TOTAL
Wong et al.[11], 2003	x	x	x	x	x	x	x	x	x	x	x	11
Bohe et al.[12], 2004	x	x		x	x	x	x	x	x	x	x	9
Antunes et al.[13], 2006	x	x	x	x	x		x	x	x	x	x	10
Falcão et al.[14], 2007	x	x	x	x	x	x	x	x	x	x		10
Falcão e Silva[15], 2008	x	x		x	x	x	x	x	x	x	x	10
Lanza et al.[16], 2008	x	x	x	x				x	x	x	x	8
Gomes et al.[17], 2012	x	x	x	x	x	x	x	x	x	x	x	10
Assumpção et al.[18], 2013	x	x		x				x	x	x	x	7

Chart 1. Characterization of the sample, variables, intervention and main results of included studies Bronchial Hygiene Technique in Newborn and Infants, 2018. (to be continued)

Author/Year	Type of Study	Sample	Variables/ Evaluation	Intervention	Main Results
ABREU et al.[19], 2006	Non-randomized clinical trial	44 preterm NB with pulmonary disease of the hyaline membranes and on mechanical ventilation (MV) with orotracheal cannula	V1: Heart Rate (HR) on the first and last day of MV V2: HR before and after intervention	Respiratory physiotherapy: postural drainage; thoracic manual vibration; thoracic percussion; diaphragmatic stimulation; passive ventilatory pattern, passive-assisted, active-assisted. Motor physiotherapy	Neonatal physiotherapy proved to be an adequate therapeutic procedure, since there was a decline in HR after interventional physiotherapy procedures with an increase in the diastolic phase of the cardiac cycle.
ANTUNES et al.[13], 2006	Randomized clinical trial	40 preterm NB in the post-extubation period	V1: HR V2: Respiratory Rate (RR) V3: Oxygen Saturation (SpO_2) *Calibrated: 5 minutes before the maneuvers; 10 and 30 minutes after the maneuvers	Group chest physical therapy (CCP): postural drainage and tapping positioned in lateral decubitus, vibrocompression and aspiration. Group increased expiratory flow (IEF): IEF slow and aspiration	IEF can be safely applied in very low, stable and post-extubation premature newborns. Its short-term effect on oxygenation is similar to CCP, with the advantage of having no repercussion in heart rate.
ASSUMPÇÃO et al.[18], 2013	Randomized and controlled clinical trial	20 infants diagnosed with congenital heart disease in postoperative cardiac surgery	V1: HR, RR, SpO_2 V2: Pain and signs of respiratory discomfort (RD) *Calibrated before and after intervention Evaluation V2: Neonatal Infant Pain Scale (NIPS) e Boletim de Silvermann-Ardersen (BSA)	Control Group: 30 minutes at rest. Intervention Group: Manual thoracic vibrocompression and aspiration	The physiotherapeutic techniques used in the studied sample did not affect the cardiorespiratory parameters of SpO2 and RR and showed no signs of pain and respiratory discomfort.
BOHE et al.[12], 2004	Randomized and controlled clinical trial	32 infants diagnosed with acute bronchiolitis	V1: Clinical score of respiratory distress (RR, HR, auscultating, use of accessory muscles and SpO_2) V2: Average length of hospital stay	Control Group: Nasopharyngeal aspiration. Intervention Group: Thoracic Physiotherapy (drainage, percussion, vibrations and nasopharyngeal aspiration)	There was no significant improvement in the clinical score of respiratory discomfort between the groups and there were no differences in the days of hospitalization between the two cohorts.
FALCÃO et al.[14], 2007	Randomized clinical trial	60 NB with respiratory disorders under routine physiotherapeutic care	V1: Pain Pain Scales: NIPS e Neonatal Facial Coding System (NFCS) * Applied before, during and after the intervention	Group 1: Manual Diaphragmatic Stimulation. Group 2: manual thoracic vibrocompression.	Manual thoracic vibrocompression was a primary source of pain, contrasting with manual diaphragmatic stimulation maneuver, with male patients expressing greater pain response.

Chart 1. Characterization of the sample, variables, intervention and main results of included studies Bronchial Hygiene Technique in Newborn and Infants, 2018. (conclusion)

Author/Year	Type of Study	Sample	Variables/ Evaluation	Intervention	Main Results
FALCÃO e SILVA.[15], 2008	Randomized clinical trial	13 NB requiring aspiration in the ICU	V1: NB containment V2: HR, SpO_2 and pain Evaluation V2: measured by parameters and NFCS	Control Group: tracheal aspiration without containment Intervention Group: tracheal aspiration associated with containment technique	Containment decreases pain and clinically stabilizes NB during tracheal aspiration procedures, since without this care aspiration can cause pain, discomfort and anxiety in the NB.
GOMES et al.[17], 2012	Randomized and controlled clinical trial	30 infants with clinical diagnosis of acute viral bronchiolitis (AVB), previously healthy, with positive respiratory syncytial virus (RSV)	V1: Wang's clinical score (retractions, RR, wheezing, and general conditions) * Values at admission, 48 and 72 hours, before and after procedures	Group 1: current physiotherapy techniques (slow and prolonged expiration and retrograde rhino pharyngeal clearance) Group 2: conventional physiotherapy techniques (modified postural drainage, expiratory compression, vibration and percussion) Group 3: aspiration of upper airways	When comparing the three protocols, the benefit was observed in current and conventional physiotherapy techniques. Moreover, current techniques have more lasting benefits.
LANZA et al.[16], 2008	Randomized clinical trial	19 infants with clinical and radiological diagnosis of bronchiolitis	V1: HR, RR, SpO_2 V2: Respiratory descomfort Evaluation V1: measured by parameters V2: BSA * Values measured before the intervention, immediately after and 15 minutes later	Group 1: vibrocompression (VC) and postural drainage Group 2: tapping (TAP) and postural drainage Group 3: Aspiration (ASP)	The use of respiratory physiotherapy techniques (VC and TAP), associated to postural drainage, in the studied sample, resulted in a reduction in respiratory discomfort and a greater elimination of secretion when compared to isolated ASP, which did not show any effectiveness.
ROCHA et al.[20], 2008	Non-randomized clinical trial	20 NB with post-extubation mucosal reabsorption atelectasis	V1: type of atelectasis V2: treatment performed after physical therapy maneuvers V3: resolution time of atelectasis	Control Group: without physical therapy treatment Intervencion Group: deep nasotracheal aspiration preceded by physiotherapeutic maneuvers	The difference in resolution time between the intervention group had an average of 2.2 hours and the control group had an average of 33.9 hours. The rate of improvement in atelectasis in the first six hours was nine times higher in the intervention group.
WONG e FOK[11], 2003	Randomized clinical trial	54 NB with atelectasis	V1: Re-expansion of atelectasis V2: Relapse of atelectasis and failure to reexpansion V3: Changes in ventilator parameters V4: Hemodynamic changes V5: Presence of pulmonary secretions V7: Intraventricular hemorrhage	Group 1: Lung Squeezing Technique (LST) protocol Group 2: PDPV (Percussion and vibration in modified postural drainage position)	LST was a useful alternative to correct atelectasis, without any additional adverse effects when compared to conventional PDPV.

Discussion

The articles studied sought to analyze the effectiveness of bronchial hygiene techniques used in NB and infants and the elements that are able to influence, and may or may not be harmful to the patient. Among the main findings were the different heart rate (HR) values after the techniques, as well as acting in the reversal of atelectasis frame, improve respiratory distress, especially in acute viral bronchiolitis (AVB) and oxygen saturation (SpO_2) resulting from treatment. Meantime, some results have demonstrated the possibility of generate pain in the NB and infants, in addition to the significant increase in HR after the intervention, which can be seen as a sign of stress.

There are still few studies on the repercussions of conventional respiratory techniques, such as manual thoracic vibration (TV), aspiration (ASP) of the upper airways, postural drainage (PD) and thoracic percussion (TP)[18]. Moreover, although most of the analyzed articles do not report data for the non-recommendation of these techniques[16, 18, 19], controversies still existing relative to their directions according to the condition of the patient, mainly because they are newborns and infants.

Inside the collected articles, the most associated maneuvers are: vibrocompression (VC), tapping (TAP), ASP and PD[14,16,18,19]. Then, to obtain satisfactory results it is important to analyze the linked procedures, given the fact that they are not performed in isolation, but rather in a set within the standard routine of the ICU[18]. In addition, the choice of the most effective technique depends on the evaluation of the physiotherapist, given the indications, contraindications and benefits that it will provide[20].

In the study by Abreu et al.[19] (2006), the comparative data of the associations of PD; mechanical and manual TV; TP; diaphragmatic stimulation; ventilatory pattern passive, passive-assisted, active-assisted and prolonged slow expiration (PSE), along with motor physical therapy, at 44 preterm NB, they demonstrated that there were no detrimental changes on the cardiorespiratory parameters. When comparing the values on the first intervention day and the last, it was possible to visualize the decrease in HR, contributing to the hemodynamic stability.

Diverging from the results found in the study by Lanza et al.[16] (2008), applied in 19 children under 2 years of age with a clinical picture of AVB and bronchial hypersecretion, there was a comparison of 3 groups divided into: VC + PD; TAP + PD; ASP. When analyzing each variable, we observed a rise in the HR values in the post-immediate physical therapy intervention, being the group 1 that obtained higher values. Although, group 2 was the one that obtained the greatest fall in cardiac values when verified 15 minutes after intervention. Even though there was a significant difference (around 2%) in SpO_2 on the 2 and 3 groups right after the intervention and after 15 minutes, the return to baseline values was quickly.

Values similar to those found by Assumpção et al.[18] (2013), when comparing the intervention group, with the VC and ASP techniques, to a control group without intervention, were performed in 20 infants with a diagnosis of congenital heart disease in the postoperative period of cardiac surgery. The results presented did not show negative repercussions on the evaluated cardiopulmonary parameters. There was an increase (2%) in SpO_2, which did not occur with the control group and were not factors triggering pain, assessed by the scale Neonatal Infant Pain Scale (NIPS).

In their study, Pereira et al.[23] (2014) affirmed, in NB, respiratory movements may be irregular, arrhythmic, intermittent and even with a change in breathing deep. Justifying the importance of the respiratory parameter being one of the most relevant, along with SpO_2, to ensure the success of the technique used. Therefore, a determinant variable for the success of the techniques is the respiratory rate (RR), being the most practical way to evaluate respiratory functional status[23].

It is important to emphasize, although other studies do not find contraindication for this use[16,18,19], the manual thoracic VC maneuver makes use of a bigger amount of pressure on the thorax, which gives more stimulus to the newborn and can generate pain[14].

In the study by Falcão et al.[14] (2007), performed in 60 NB, NIPS and Neonatal Facial Coding System (NFCS) scales were applied in two groups: one receiving manual diaphragmatic stimulation and another

receiving VC. The analysis of the scores obtained on the scales showed that VC had a painful reaction. While in manual diaphragmatic stimulation, the maximum value reached from the median was equal to three, which does not attest to the presence of pain, but indicates that it may interfere with pre-existing painful processes.

Neonatal and pediatric pain has high difficulty to be identified, requiring care and special attention, such as instruments to decode their language and assist on the understanding of their manifestations[24]. Understanding how these procedures or manipulations can tease or potentiate the response of the newborn and the infant is of bigger clinical relevance, since the pediatric patient doesn't know how verbalize their painful sensation[18].

In the results obtained by Antunes et al.[13] (2006), there was a comparison between two groups divided into conventional respiratory physiotherapy (CRP), which included PD, TAP, being positioned in the right and left lateral decubitus, VC and ASP; group increased expiratory flow (IEF): IEF slow and aspiration, applied in 40 preterm newborns divided equally. The both groups had a satisfactory rise in SpO_2, when analyzed for HR, the CRP group showed a significant rise over 30 minutes, which can be seen as a sign of stress, generating more respiratory discomfort.

In the study conducted by Falcão and Silva[15] (2008), 13 NB admitted to the ICU who needed tracheal ASP were included. All of they passed for two methods, with order draw: tracheal ASP, without any other intervention (control group), and tracheal ASP with the containment technique (intervention group). When HR and SpO_2 values were analyzed, the intervention group had positive values. Concerning the presence of pain, three neonates presented pain during the procedure when contained, and twelve presented pain when not contained.

Another relevant point is the presence of atelectasis, defined as a collapse of a segment, lobe or the whole lung, causing a decrease in lung volume and a change in ventilation/perfusion relation[25]. There is no consensus on the ideal technique to be used in the atelectasis intervention groups in newborn[20].

In the study performed by Rocha et al.[20] (2008), 20 NB with atelectasis of reabsorption by mucus buffer after extubation were analyzed, equally separated into the control group and the intervention group (deep nasotracheal ASP and respiratory physiotherapy). The analysis of this study showed there was a favorable success for the intervention and, when compared to the control group, there was a higher percentage of resolution of atelectasis in the first 6 hours.

In the results obtained by Wong and Fok[11] (2003), the lung squeezing technique (LST) was more effective than percussion and vibration in modified PD (PDPV) for re-expansion of atelectasis. Were analyzed preterm NB randomized into an experimental group (n = 26) treated with the LST and a control group (n = 30) treated with PDPV. After the first therapy session, full lung re-expansion occurred in 81% of the LST group and in only 23% of the PDPV group and there was no significant difference in hemodynamic disorders.

Another aspect with disagreement is the correct indication of respiratory physiotherapy to the treatment of AVB, defined as an acute inflammatory disease of the lower respiratory tract when an infection of the bronchiolar epithelium occurs. Some authors do not indicate respiratory physiotherapy in the acute phase because bronchial hygiene maneuvers cause agitation in the child and may increase hypoxemia and bronchospasm[4].

In research conducted by Bohe et al.[12] (2004), 32 infants diagnosed with AVB were divided into a control group in which only occurred ASP nasopharyngeal and a group which occurred respiratory physiotherapy (PD, TAP, vibration and nasopharyngeal ASP). The respiratory difficulty score, obtained with the variables described in Chart 1, and the mean length of hospital stay were compared, both assessed during admission and discharge. The medians obtained showed the physiotherapy didn't contribute to a significant benefit between the groups and did not present difference in the days of hospitalization.

Refuted these values, Gomes et al.[17] (2012), demonstrated results proving the benefit of using respiratory therapy. Over 30 infants with AVB and positive for respiratory syncytial virus (RSV) were compared

in three groups: new chest physical therapy (prolonged slow expiration and clearance rhinopharyngeal retrograde), conventional chest physical therapy (modified PD, expiratory compression, vibration and percussion) and ASP of the upper airways. With the Wang clinical score measured at admission, 48 and 72 hours after the procedures; it was possible observe reduce in respiratory discomfort in both physiotherapy techniques. The most effective technique was the new chest physical therapy, because after 72 hours, besides the constant decrease of the score, it showed highing in SpO_2 (2%).

Conclusion

With the analysis of the studies found in this review, it's possible to conclude the bronchial hygiene techniques, within respiratory physiotherapy, are effective in improving respiratory discomfort and increasing SpO_2 in the treatment of NB and infants. Current techniques have shown greater efficacy over conventional, they presented greater durability in the respiratory values, didn't interfere in the HR and greater speed in the reversion in the atelectasis.

There are differences between the authors about the benefits and harms, with different results of influence these maneuvers on the patients HR. They found that a highing in HR occurs soon after the intervention, even though vast majority showed a rapid decrease or remained stable. Among the techniques that presented greater easiness to cause and to endure this increase is the VC, which can be seen as a sign of stress, generating pain.

The lack of standardization in the use of maneuvers causes conflict to better analysis, since each author made use of different techniques and in different ways. When compared that use in the same pathology, don't exist consensus as to the number and order of correct procedures.

In that way, it is recommended more studies need to be done to standardizing the techniques used, facilitating a complete investigation of the generated effects, being positive and negative. Consequently, providing insurance care the NB and the infant in the midst of vulnerability present, leading to the growth of respiratory physiotherapy with proven intervention.

Author contributions

Oliveira TC participated in the study design, the search and selection of research data, interpretation of results and writing. Moda GSM participated in the search and selection of research data, construction of the discussion of the scientific article. Ribeiro AKPL supervised the study and participated in the writing. Nunes SED, Araújo RA and Gaia VSC supervised the study.

Competing interests

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

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