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Frederico Jorge de César Ramos Pinto

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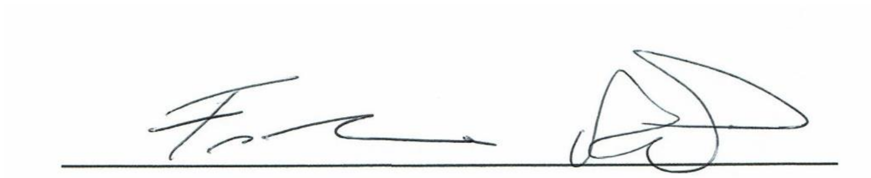
Esta tese foi escrita de acordo com a legislação e regulamentos aplicáveis ao Doutoramento em Ciências Biomédicas: Regulamento Geral dos Terceiros Ciclos de Estudos da Universidade do Porto, aprovado por despacho reitoral de 10 de abril de 2015 e publicado em Diário da República, 2ª série, nº 90 de 11 de maio de 2015, por Despacho nº 4889/2015. Decreto-lei nº 63/2016 – Diário da República nº 176/2016, Série I de 13 de setembro de 2016 do Ministério da Ciência, Tecnologia e Ensino Superior. Plano de estudos do doutoramento em Ciências Biomédicas, do Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto.

Declaração de Honra

Declaro que a presente tese é de minha autoria e não foi utilizada previamente noutro curso ou unidade curricular, desta ou de outra instituição. As referências a outros autores (afirmações, ideias, pensamentos) respeitam escrupulosamente as regras da atribuição, e encontram-se devidamente indicadas no texto e nas referências bibliográficas, de acordo coma s normas de referenciação. Tenho consciência de que a prática de plágio e auto-plágio constitui um ilícito académico.



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De acordo com o disposto no ponto n.º 2 do Art.º 31º do Decreto-Lei n.º 74/2006, de 24 de março, aditado pelo Decreto-Lei n.º 230/2009, de 14 de setembro, o autor declara que na elaboração desta tese foram incluídos dados das publicações abaixo indicadas. O autor participou ativamente na conceção e execução dos trabalhos que estiveram na origem dos mesmos, assim como na sua interpretação, discussão e redação.

According to the relevant national legislation, the author declares that this thesis includes data from the publications indicated below. The author participated actively in the conception and execution of the work that originated that data, as well as in their interpretation, discussion and writing.

The following articles were used to write this thesis:

- **Pinto, F. R.**, Correia-Costa, L., & Azevedo, I. (2020). Comparison of Kristjansson Respiratory Score and Wang Respiratory Score in infants with bronchiolitis in a hospital emergency department. *Hong Kong Physiotherapy Journal, 40*, Article 2. https://doi.org/10.1142/S1013702520500146

- **Pinto, F. R.**, Alexandrino, A. S., Correia-Costa, L., & Azevedo, I. (2020). Ambulatory chest physiotherapy in mild-to-moderate acute bronchiolitis in children under two years of age – a randomised controlled trial. *Hong Kong Physiotherapy Journal, Vol. 41, No. 2 (2021) 1–10.* https://doi.org/10.1142/S1013702521500098

> “O conhecimento tem o dom de se multiplicar quando nos propomos a ampliá-lo.”
>
> Jorge Sabonji

À Carla, pelo exemplo de perseverança ao longo destes últimos anos.

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ABSTRACT

Introduction: Bronchiolitis is one of the main causes of admission to hospital emergency departments in children up to 2 years of age, contributing to an overload for families and health care services. Most cases are mild to moderate in severity, being referred to outpatient treatment. Treatment is mainly supplemental oxygen (O_2) and nutritional support, and international guidelines do not recommend chest physiotherapy for the management of bronchiolitis. However, the emergence of new techniques in bronchial clearance has created an increase interest on chest physiotherapy intervention in bronchiolitis. In order to investigate the role of chest physiotherapy in the treatment of bronchiolitis in an outpatient basis we conducted two studies.

Objectives: In Study 1 we compared two severity scores, the Kristjansson Respiratory Score (KRS) and Wang Respiratory Score (WRS), that assess the severity of bronchiolitis, to find out which score has the best psychometric properties, in order to choose the best score for the second study. In Study 2, a controlled randomized trial, we aimed to investigate the efficacy of chest physiotherapy in the treatment of mild to moderate bronchiolitis, on an outpatient basis. In this study, we sought to find out if the group that had chest physiotherapy improved more their clinical status, obtaining lower values on the respiratory severity score, compared to a non-intervention group.

Methods: In Study 1, observational prospective, the KRS and WRS scales were applied at the time of admission to the emergency room, and at the time of decision to hospitalize or discharge to outpatient care, by the doctor who assisted the child and the physiotherapist. Both scales were applied in 60 children, aged less than 2 years, with a clinical diagnosis of bronchiolitis, admitted in the paediatric emergency department (PED) of a tertiary care hospital, Centro Hospitalar Universitário São João (CHUSJ).

In study 2, carried out in the same PED and using KRS to assess the severity of bronchiolitis, a total of 105 children were assessed for eligibility to participate in the present study. Due to the exclusion criteria, only 80 children were selected and randomly assigned to the intervention group (IG, n = 42) and to the control group (CG, n = 38). Due to loss of follow-up or subsequent hospital admission, a total of 45 children completed the study (IG, n = 28; CG, n = 17). Severity was assessed by oxygen saturation (SpO_2) and by the KRS, on admission to the emergency room, at discharge and during the follow-up visits. IG children underwent 20-minutes session of chest physiotherapy daily (5 sessions) during the first week, and every other day (3 sessions)

during the second week. The techniques used were prolonged slow exhalation (PSE), retrograde rhinopharyngeal clearance (RRC) and provoked cough (PC).

Results: In study 1, inter-rater reliability was higher in KRS (ICC 0.78) comparatively with WRS (ICC 0.69) and the Cronbach α and weighted kappa had similar values in KRS versus WRS. This allows us to conclude that KRS would have more consistent results in the assessment of bronchiolitis' level of severity by health personnel in a busy hospital emergency room, being the score chosen to assess severity in study 2.

In the study 2, after two weeks of follow-up, there was a significant improvement in the KRS in the IG compared to the CG at Day 15 with mean difference (95%CI) of -0.9 (-1.6 to -0.3).

Conclusion: We found that KRS is a good score to access bronchiolitis severity in PED and chest physiotherapy had a beneficial effect on the respiratory health condition of children with mild-to-moderate bronchiolitis, treated on an outpatient basis. Further studies are needed in order to deepen the research of the impact of chest physiotherapy as part of the treatment of bronchiolitis, hopefully reinforcing our findings that chest physiotherapy, on an outpatient basis, is an asset in the treatment of mild to moderate cases.

RESUMO

Introdução: A bronquiolite é uma das principais causas de admissão nos serviços de urgência hospitalar em crianças até aos 2 anos de idade, contribuindo para uma sobrecarga para as famílias e para o serviço nacional de saúde. A maioria dos casos são de gravidade ligeira a moderada, sendo encaminhados para tratamento ambulatorial. O tratamento é principalmente de oxigénio (O2) suplementar e apoio nutricional, e as diretrizes internacionais não recomendam fisioterapia respiratória para o tratamento da bronquiolite. Contudo, o aparecimento de novas técnicas de desobstrução brônquica criou um interesse crescente na intervenção da fisioterapia respiratória na bronquiolite. A fim de investigar o papel da fisioterapia respiratória no tratamento da bronquiolite em regime ambulatório, foram realizados dois estudos.

Objetivos: No Estudo 1 comparamos duas escalas de severidade, a Kristjansson Respiratory Score (KRS) e a Wang Respiratory Score (WRS), que avaliam a severidade da bronquiolite, para descobrir qual a escala com melhores propriedades psicométricas, a fim de escolher a melhor escala a ser utilizada no segundo estudo. No Estudo 2, um ensaio randomizado controlado, o nosso objetivo era investigar a eficácia da fisioterapia respiratória no tratamento da bronquiolite leve a moderada, num regime ambulatório. Neste estudo, procurou-se descobrir se o grupo que tinha intervenção de fisioterapia respiratória melhorou mais o seu estado clínico, obtendo valores mais baixos na pontuação de severidade respiratória, em comparação com um grupo controlo.

Métodos: No Estudo 1, prospetivo observacional, as escalas KRS e WRS foram aplicadas no momento da admissão no serviço de urgência, e no momento da decisão de hospitalização ou alta para cuidados ambulatórios, pelo médico que assistiu a criança e pelo fisioterapeuta. Ambas as escalas foram aplicadas a 60 crianças, com menos de 2 anos de idade, com diagnóstico clínico de bronquiolite, admitidas no serviço de urgência pediátrica (SUP) de um hospital central, Centro Hospitalar Universitário São João (CHUSJ).

No estudo 2, realizado no mesmo SUP e utilizando a KRS para avaliar a severidade da bronquiolite, foram avaliadas um total de 105 crianças, elegíveis para o presente estudo. Devido aos critérios de exclusão, apenas 80 crianças foram selecionadas e atribuídas aleatoriamente no grupo de intervenção (GI, n = 42) e no grupo de controlo (GC, n = 38). Devido à perda de acompanhamento ou subsequente admissão hospitalar, um total de 45 crianças completaram o estudo (IG, n = 28; CG, n = 17). A severidade foi avaliada pela saturação de oxigénio (SpO2) e pela pontuação da KRS, na admissão ao serviço de urgência, na alta e durante as sessões em ambulatório. As crianças do GI foram submetidas, diariamente, a uma sessão de 20 minutos de fisioterapia respiratória (5 sessões) durante a primeira semana, e em dias alternados (3 sessões) durante a segunda semana. As técnicas utilizadas foram a expiração lenta prolongada (ELPr), a desobstrução rinofaringe retrógrada (DRR) e a tosse provocada (TP).

Resultados: No estudo 1, a fiabilidade interobservador foi mais alta na KRS (ICC 0,78) comparativamente com a WRS (ICC 0,69). O α de Cronbach e o valor de Kappa ponderado obtiveram valores semelhantes na KRS versus WRS. Isto permitiu concluir que a KRS obteve resultados mais consistentes na avaliação do nível de severidade da bronquiolite por diferente pessoal de saúde, numa sala de urgências hospitalar movimentada, sendo a escala escolhida para avaliar a severidade no estudo 2.

No estudo 2, após duas semanas de acompanhamento, houve uma melhoria significativa da KRS no GI em comparação com o GC ao 15º dia, com uma diferença da média (95%CI) de -0,9 (-1,6 a -0,3).

Conclusão: Verificou-se que a KRS é uma escala boa para avaliar a severidade da bronquiolite num SUP e que a fisioterapia respiratória teve um efeito benéfico no estado de saúde das crianças com bronquiolite leve a moderada, tratadas em regime ambulatório. São necessários mais estudos a fim de aprofundar os resultados do impacto da fisioterapia respiratória como parte do tratamento da bronquiolite, reforçando as nossas conclusões de que a fisioterapia respiratória, numa base ambulatória, é uma vantagem no tratamento de casos ligeiros a moderados.

TABLE OD CONTENTS

List of abbreviations / Acronyms

AAP – American Academy of Paediatrics

BRAS – Bronchiolitis Risk of Admission Score

BRS – Bronchial Respiratory Sound

CG – Control group

CHWRS – Children's Hospital of Wisconsin Respiratory Score

EFA – Expiratory flow acceleration

HR – Heart rate

ICC – intraclass-correlation coefficient

IG – Intervention group

KRS – Kristjansson respiratory score

MTS – Modified Tal Score

NBS – Normal Breathing Sound

O_2 – Oxygen

PC – Provoked Cough

PED – Paediatric emergency department

PEP – Point of equal pressure

P_{pl} – Pleural pressure

PSE – Prolonged slow expiration

RDAI – Respiratory Distress Assessment Instrument

RDS – Respiratory Distress Score

RIS – Respiratory Index Score

RR – Respiratory rate

RRC – Retrograde rhinopharyngeal clearance

RSL – Respiratory Score of Liu

RSV – Respiratory Syncytial Virus

SpO_2 – Oxygen Saturation

WRS – Wang respiratory score

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INTRODUTION

Acute viral bronchiolitis has a high incidence in the first two years of life and, despite being generally a mild to moderate self-limiting condition, it has a huge impact on healthcare care services, both in the hospital and outpatient settings. Bronchiolitis is one of the main causes for non-scheduled visits to hospital emergency departments and admissions to hospital (Bryan et al., 2017; Direção Geral da Saúde, 2012; Fontoura-Matias et al., 2020; Mendes-da-Silva et al., 2019).

The main causal infectious agent is the respiratory syncytial virus (RSV), but others less frequent agents, such as rhinovirus, parainfluenza type 3, metapneumovirus, adenovirus and mycoplasma pneumoniae may also cause bronchiolitis (Antunes et al., 2010; Borges et al., 2019; Gil et al., 2018; Mação et al., 2011; Neves Barreira et al., 2001; Schaap-Nutt et al., 2012; Smyth, 2007; Van Ginderdeuren et al., 2017). The diagnosis is mainly based on clinical history and physical examination, and laboratory tests or radiological images are not routinely recommended. The main signs and symptoms of bronchiolitis are rhinorrhoea, cough, tachypnoea, chest retractions and crackles on auscultation (Baraldi et al., 2014; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Silver & Nazif, 2019). This picture reflect an obstruction of the airways, due to the increase of secretions, provoked by the viral infection, reducing its conductance and leading to an increase in the respiratory effort (Silver & Nazif, 2019; Smyth, 2007).

The treatment of bronchiolitis is still controversial and guidelines recommend mostly supportive measures (Direção Geral da Saúde, 2012; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014). Supplemental oxygen (O_2) is usually recommended when oxygen saturation (SpO_2) is below 90%; when the child shows signs of dehydration due to decreased food intake, oral or intravenous hydration is recommended (Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014). The use of medications such as bronchodilators, corticosteroids, mucolytics and antibiotics is not recommended in guidelines (Direção Geral da Saúde, 2012; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Roque i Figuls et al., 2016). Chest physiotherapy has been used through various techniques but its efficacy has been questioned and thus it is not recommended in guidelines. However, the evidence of chest physiotherapy intervention in bronchiolitis has evolved, and its efficacy is again a matter of debate. At the end of the XX century, new chest physiotherapy techniques emerged, developed by the physiotherapist Guy Postiaux, to assist mucociliar clearance mechanisms, reduce bronchial obstruction and improve the clinical status of children with bronchiolitis (Postiaux et al., 1997). To date, few studies have been carried out with the new techniques of prolonged slow expiration (PSE), provoked cough (PC) and retrograde rhinopharyngeal clearance (RRC), compared to the countless studies including the use of classic techniques (clapping; postural drainage; vibration) and expiratory flow acceleration (EFA). Because studies with classical techniques and EFA did not show beneficial results, such as decreasing the severity of breathing difficulties or the length of hospital stay, several literature reviews concluded that chest physiotherapy was not a treatment to be applied in bronchiolitis (Perrotta et al., 2005, 2007; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Roque i Figuls et al., 2012; Roque i Figuls et al., 2016). Nevertheless, more recently a few published studies and the latest Cochrane review on the role of chest physiotherapy in bronchiolitis demonstrated that the application of PSE, PC and RRC improves scores of respiratory severity and bronchial clearance (Conesa-Segura et al., 2019; Gomes et al., 2012; Remondini et al., 2014; Rochat et al., 2012; Roque i Figuls et al., 2016).

As most cases of bronchiolitis, which resort to the emergency department, are referred to home management and because all studies about the intervention of chest physiotherapy in bronchiolitis have been carried out with hospitalized children, the present thesis was developed to answer the following question - is chest physiotherapy beneficial in the treatment of bronchiolitis in children up to 2 years of age, on an outpatient basis?

This thesis consists of two studies. In Study 1, 60 children aged between 0 and 2 years old with a diagnosis of bronchiolitis were evaluated using two scores of respiratory severity. The selection of the scores was decided after a research of scores designed specifically for bronchiolitis and with an evaluation of inter-rater reliability. This criterion was essential because all children in the first and second study would be evaluated by two health professionals (a physician and a physiotherapist), and it is essential that both evaluations were similar. The scores chosen were the Wang Respiratory Score (WRS) (Wang et al., 1992) and the Kristjansson Respiratory Score (KRS) (Kristjansson et al., 1993) (Chapter 2).

In Study 2, carried out in the same paediatric emergency department (PED) and using KRS to assess the severity of bronchiolitis, a total of 105 children were assessed for eligibility to participate in the present study. However, due to the exclusion criteria and because some of them were admitted at the inpatient ward, 80 children were finally included and randomly assigned to the intervention group (IG) (n = 42) and to the control group (CG) (n = 38). Due to discontinuation of follow-up or subsequent hospital admission, a total of 45 children completed the study (IG, n = 28; CG, n = 17) (Fig. 1). This reduction was mainly due to the loss of follow-up visits for assessment and treatment. In the IG, the physiotherapy techniques chosen were PSE, RRC and PC, as they are the most recent techniques and have shown to present good results in the clearance of secretions and improvement of bronchial obstruction.

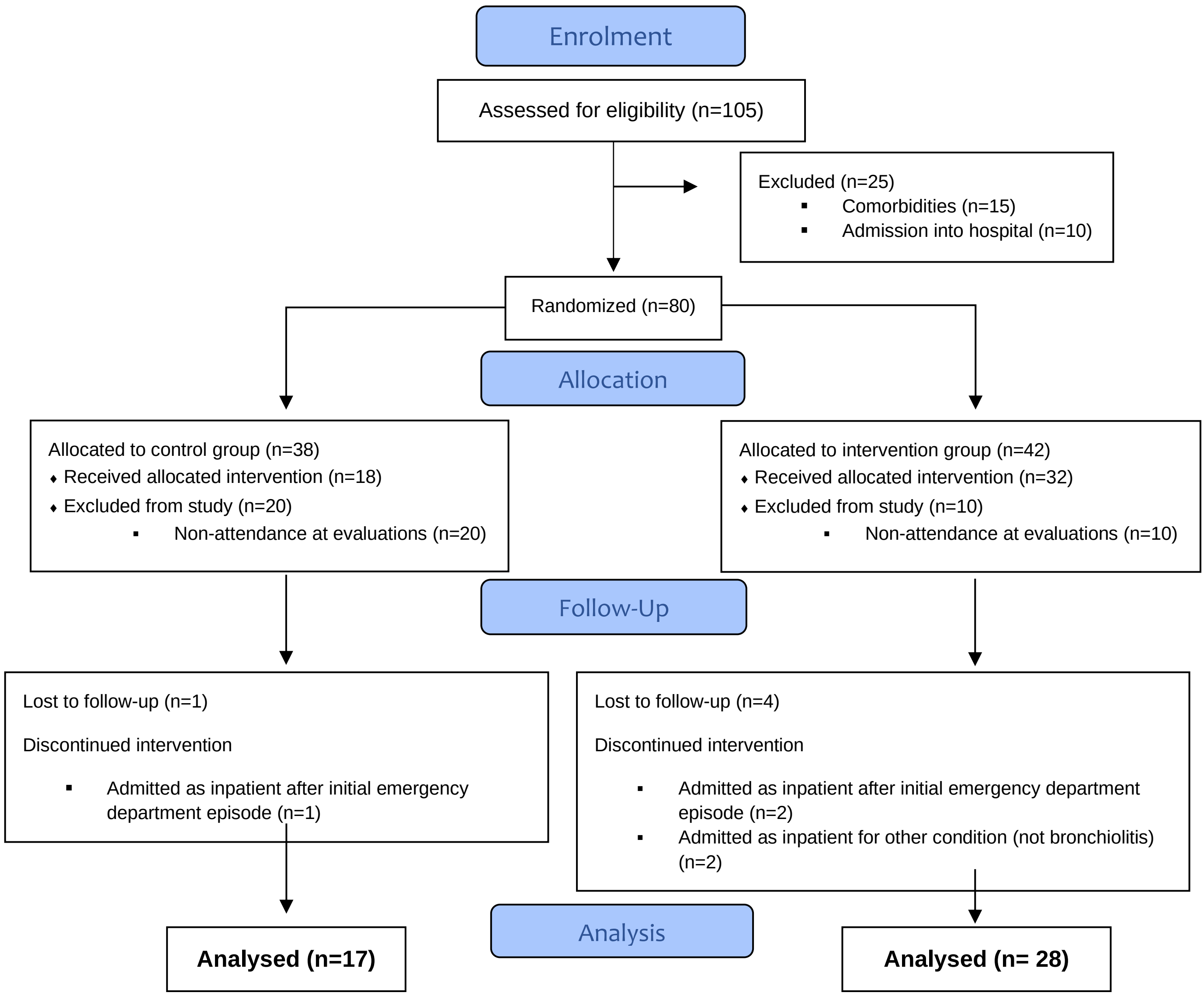

Figure 1 - Screening, Random Assignment, and Follow-up of intervention and control group.

As main objective, this thesis sought to understand the impact of chest physiotherapy on children with bronchiolitis, observed in a hospital PED and treated on an outpatient basis.

In chapter 1, pulmonary anatomophysiology and, more specifically, children's pulmonary anatomophysiology will be addressed. The internationally accepted definition of bronchiolitis, its pathogenesis, the assessment tools currently available, and the recommended treatment options will be discussed. Finally, the role of chest physiotherapy in the treatment of bronchiolitis will be described, as well as the techniques used and the evaluation protocol implemented.

Chapters 2 and 3 consist of the study 1 (evaluation of inter-rater reliability of two bronchiolitis severity scores) and study 2 (randomized study of chest physiotherapy in bronchiolitis in an outpatient setting), as previously described.

Finally, in chapter 4, a general discussion of the results, along with methodological considerations, discussion of study's strengths and limitations and final conclusion remarks are presented.

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CHAPTER 1 – LITERATURE REVIEW

1. PULMONARY ANATOMOPHYSIOLOGY

The pulmonary system has two types of airways. The extra thoracic ducts, constituted by the nasal cavities, nasopharynx, oropharynx, larynx and trachea, and the intra thoracic ducts. The intra thoracic pathways begin when the trachea divides into two branches, forming the main (primary) bronchi and they divide into several bronchial branches, with an ever-smaller calibre until the formation of the bronchioles and these are terminated by the alveolar sacs (Fig. 1).

THE TRACHEA extends from the larynx (level of the sixth cervical vertebra) to the middle of the chest (level of the fifth thoracic vertebra), leading the air to the two main bronchi (Ross & Pawlina, 2010; Williams et al., 1995). A unique feature of the trachea is the presence of a series of C-shaped hyaline cartilages, stacked on top of each other to form a support structure, allowing the lumen of the trachea to remain open (Bustamante-Marin & Ostrowski, 2017; Ross & Pawlina, 2010). It is this structure that prevents tracheal collapse, particularly during expiration. Fibroelastic tissue and smooth musculature, fill the gap between the free ends of the C-shaped cartilages in the posterior portion of the trachea, adjacent to the oesophagus. The tracheal epithelium is similar to the respiratory epithelium in other parts of the conducting airways (bronchial tree), being constituted by ciliated cells, mucous cells (calyx) and basal cells. Brush cells are also present, but in small numbers, as well as the small granular cells (Bustamante-Marin & Ostrowski, 2017; Ross & Pawlina, 2010).

Fundamental to the mucociliar cleaning mechanism, ciliated cells extend throughout the tracheal epithelium to the respiratory bronchioles (Bustamante-Marin & Ostrowski, 2017; Sleigh et al., 1988). The cilia move in a coordinated and sweeping manner (metachronic movement), across the mucous lining of the airways (upper and lower), in the periphery-centre direction (Sleigh et al., 1988). A disturbance of the ciliary beat, especially in the middle or distal airways, can cause an accumulation of mucus (Cohen, 2006). This accumulation promotes local microbial proliferation, easily leading to infection and inflammatory response. Ciliary movement, namely transport speed, tends to decrease with age, slows down during sleep and is stimulated with physical exercise (Cohen, 2006; Houtmeyers et al., 1999; Wolff et al., 1977). The frequency of ciliary beat decreases from the trachea towards the bronchioles, which can facilitate the accumulation of secretions in the peripheral pathways (Houtmeyers et al., 1999; Postiaux, 2004; Sedaghat et al., 2016). This frequency also varies depending on the temperature and humidity. Mucociliar drainage decreases with age (due to reduced ciliary movement) and some studies report that it is faster in females (Houtmeyers et al., 1999; Postiaux, 2004; Sedaghat et al., 2016).

BRONCHI, are often anatomically described as right and left bronchi. Upon entering the pulmonary hilum, each major bronchi divides into lobar bronchi (secondary bronchi) and these into segmental bronchi (tertiary bronchi) (Ross & Pawlina, 2010; Williams et al., 1995).

Initially, the histology of bronchi is similar to that of trachea. Cartilage rings are replaced by irregularly shaped cartilage plates, giving the bronchi a circular or cylindrical shape in contrast to the ovoid shape of the trachea. The other difference of the bronchial wall is the addition of smooth musculature, forming a circumferential layer becoming more and more present as the amount of cartilage decreases (Ross & Pawlina, 2010).

BRONCHIOLES are the end of the tubular system that constitutes the bronchial tree, being responsible for ventilating the pulmonary lobes. The lobes are constituted by what are called pulmonary acini, which are the smallest structural units, consisting of a terminal bronchioles, respiratory bronchioles and alveoli. It is the smallest pulmonary functional unit, being called the bronchiolar respiratory unit (Ross & Pawlina, 2010).

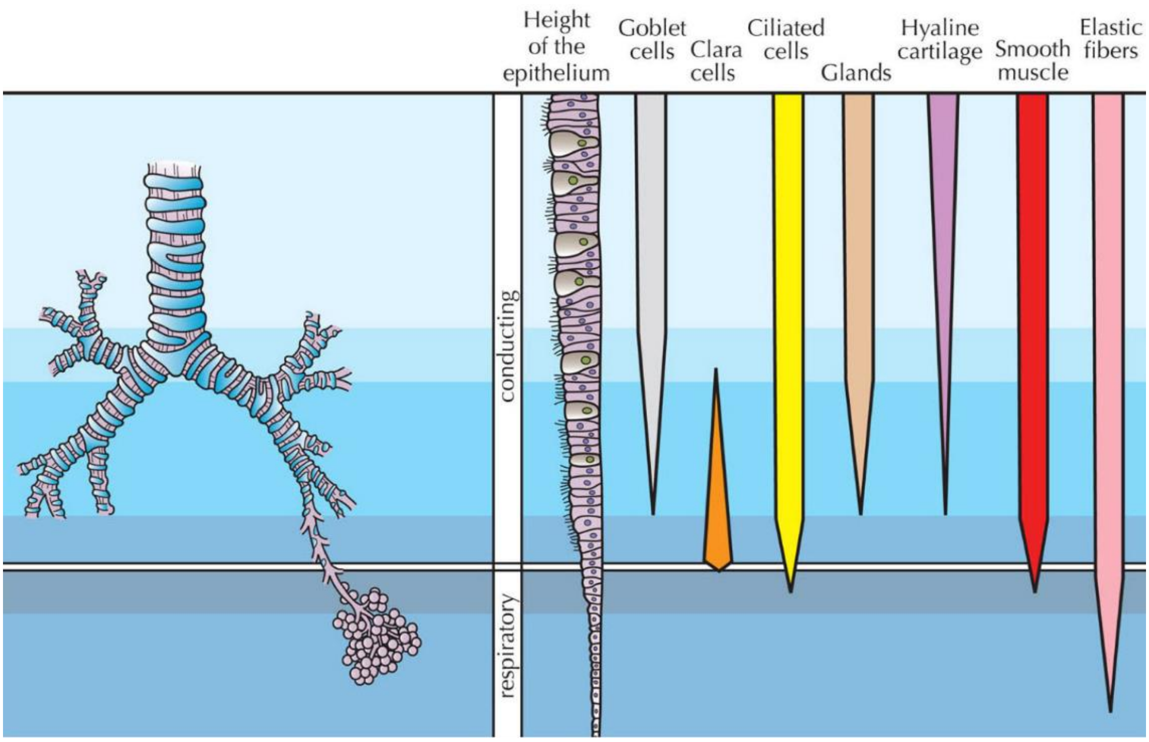


Fig. 1: Distribution of different types of tissues along the bronchial tree. Image adapted from the site *https://www.wikiwand.com/en/Respiratory_tract#/Lower_respiratory_tract*

ALVEOLES are the end of the bronchial tree. They are responsible for exponentially increasing the surface area available for gas exchange, from the inspired air, with the body blood (Ross & Pawlina, 2010; Williams et al., 1995). If the bronchi and bronchioles keep the lumen open due to the existence of cartilage on their walls, the alveoli are able to maintain their bag shape due to the presence of the **surfactant** - a liquid produced by the alveoli itself, which reduces the internal surface tension in the alveolar wall, through of a thin aqueous layer that covers the pulmonary epithelium, actively participating in the elimination of foreign materials and playing a crucial role in the alveolar immune response (Davis & Mychaliska, 2013; Garcia-Mouton et al., 2019; Otis et al., 1993; Ross & Pawlina, 2010).

An important characteristic is the existence of communications between adjacent alveoli, parallel bronchioles and between these and the alveoli, through pores between the walls of alveoli (Kohn pores), channels between the respiratory bronchioles (Lambert channels) and channels between the respiratory bronchioles and alveoli (Martin channels), which is called **collateral ventilation** - this allows air to circulate between the alveoli and respiratory bronchioles. Kohn's pores can be of great importance in some pathologies, such as obstructive pulmonary disease that blocks the normal airway passage to the alveoli. Because these pores exist, the inspired air can reach the alveoli, even if there is an airway blockage (Gompelmann et al., 2013; Postiaux et al., 2018; Ross & Pawlina, 2010).

An important aspect of the respiratory system, in addition to those already mentioned, is the presence of a liquid substance, from the nasal cavities to the terminal bronchioles. This substance, called **mucus**, is formed in the surface epithelial cells and in the submucosal glands. Mucus is a remarkable polysaccharide, with properties between a viscous liquid and an elastic solid (rheological properties). It is formed by two overlapping layers: the deep layer, liquid, fluid layer, allows the vibrating lashes to beat, and the superficial layer, gel type, viscous, not soluble in water, which is displaced by the tips of the cilia, in the direction of the periphery to the centre of the bronchial tree (trachea) (Dickey, 2018; Sahin-Yilmaz & Naclerio, 2011). The mucus has three functions: first, it is a barrier mechanism, trapping particles in the liquid covering of the epithelial surface of the airways and eliminating them from the bronchial tree by ciliary action; second, it acts as a chemical screen, having antioxidant properties; third, it forms a biological barrier, interacting with microorganisms and luminous inflammatory agents, preventing them from adhering and migrating through the airway epithelium (Sleigh et al., 1988; Wanner et al., 1996). When it reach the trachea, as well as mucus from the upper airways that travels to the glottis, they are swallowed and eliminated by the gastrointestinal tract (Dickey, 2018; Sahin-Yilmaz & Naclerio, 2011).

The rheological properties of mucus, its viscoelasticity, which allows it to move through the bronchial lumen, decrease due to the increase in the amplitude and duration of the request to which the mucus is subjected (ciliary beat; cough) (Sleigh et al., 1988). If the level of the lower layer exceeds its normal depth, the ciliary tips are unable to interact properly with the upper layer of mucus. On the other hand, if the level is very low, the mucus itself (upper layer) prevents the ciliary beating, with no movement of secretions towards the trachea (Smith et al., 2008; Wanner et al., 1996). That is, the mucus must have a low viscosity and high elasticity to be transported by the cilia. Conversely, when viscosity increases or decreases a lot, mucus is poorly transported (Cohen, 2006; Postiaux, 2004; Smith et al., 2008).

The **lung circulatory system** is divided into two circulations: **Pulmonary circulation** - responsible for passing venous blood through the alveoli, so that there is an exchange of gases between the outside and the inside of the organism and the blood is oxygenated. This circulation derives from the pulmonary artery, goes to the arterial capillaries of the alveolar septum, continues through the pulmonary venous capillaries, which join to form venules and these form the four pulmonary veins that return blood to the heart (Ross & Pawlina, 2010; Williams et al., 1995). The second circulation, **Bronchial circulation** - is formed by the bronchial arteries that come from a branch of the aorta and supply arterial blood to all lung tissue, except the alveoli (that is, the walls of the bronchi and bronchioles and the connective tissue of the lung, except the alveolar septum). The thinner branches of the bronchial arteries connect with the pulmonary capillaries, allowing the bronchial and pulmonary circulations to connect (Ross & Pawlina, 2010; Williams et al., 1995). Associated with the lung circulatory system is the lymphatic system, formed by a set of lymphatic vessels, which drain the lung parenchyma and follow the airways to the hilum. Lymph nodes are found along the route of the large lymphatic vessels. A second set of lymphatic vessels drains the surface of the lung and circulates in the connective tissue of the visceral pleura, a serous membrane made up of a surface of mesothelium and underlying connective tissue (Ross & Pawlina, 2010; Williams et al., 1995).

Pulmonary innervation consists of post-ganglionic sympathetic fibres that originate in the sympathetic trunks, ending in the bronchial tree, the pulmonary vessels and the bronchial tree glands. These sympathetic fibres have the function of creating the stimulus for bronchodilation, vasoconstriction and inhibition of secretory glands. Together with these sympathetic fibres there are the pre-ganglionic parasympathetic fibres, which receive innervation from the vague nerve (X cranial nerve), which will innervate the smooth muscles of the bronchial tree, the pulmonary vessels and the bronchial glands. The functions of parasympathetic fibres are the stimulus for bronchoconstriction, vasodilation and the stimulation of secretory glands (Ross & Pawlina, 2010; Williams et al., 1995).

2. PULMONARY ANATOMOPHYSIOLOGY IN CHILDREN

The anatomophysiology of the child's respiratory system has important particularities that justify the need for its description. These are the particularities that led to the need to create new drainage and bronchial clearance techniques, since the adaptation of the techniques used in children over two years of age and in adults, did not have positive effects in younger children.

The child up to 2 years old has a respiratory system with anatomical differences in the upper and lower airways. At birth, the new-born's larynx occupies a high position in the neck, with the lower edge of the cricoid cartilage positioned at an intermediate level between the third and fourth cervical vertebrae (C3 and C4), descending to the level of C7 at age 5 (Moss, 1965). As the larynx is raised, the trachea is more exposed, allowing its manipulation (pressure point of the provoked cough) without risk of injuring the larynx, which constitutes the upper sphincter of the respiratory system (protects the lungs from inhalation of foreign bodies) (Postiaux, 2004; Wadie, 2012).

Lung development starts in the embryonic phase of the foetus (Fig. 2) and is continued in the postnatal period. Regarding the bronchial tree itself, the child from birth to 8 years of age goes through a period of very significant structural growth, especially up to 2 years of age (Bush, 2016; Davis & Mychaliska, 2013). Conventionally, it can be said that alveolar growth occurs mainly in the postnatal period, with a rapid initial phase in the first 2 years of life and a much slower phase until the age of 8, when the alveoli increase in size, but not in number (Bush, 2016).

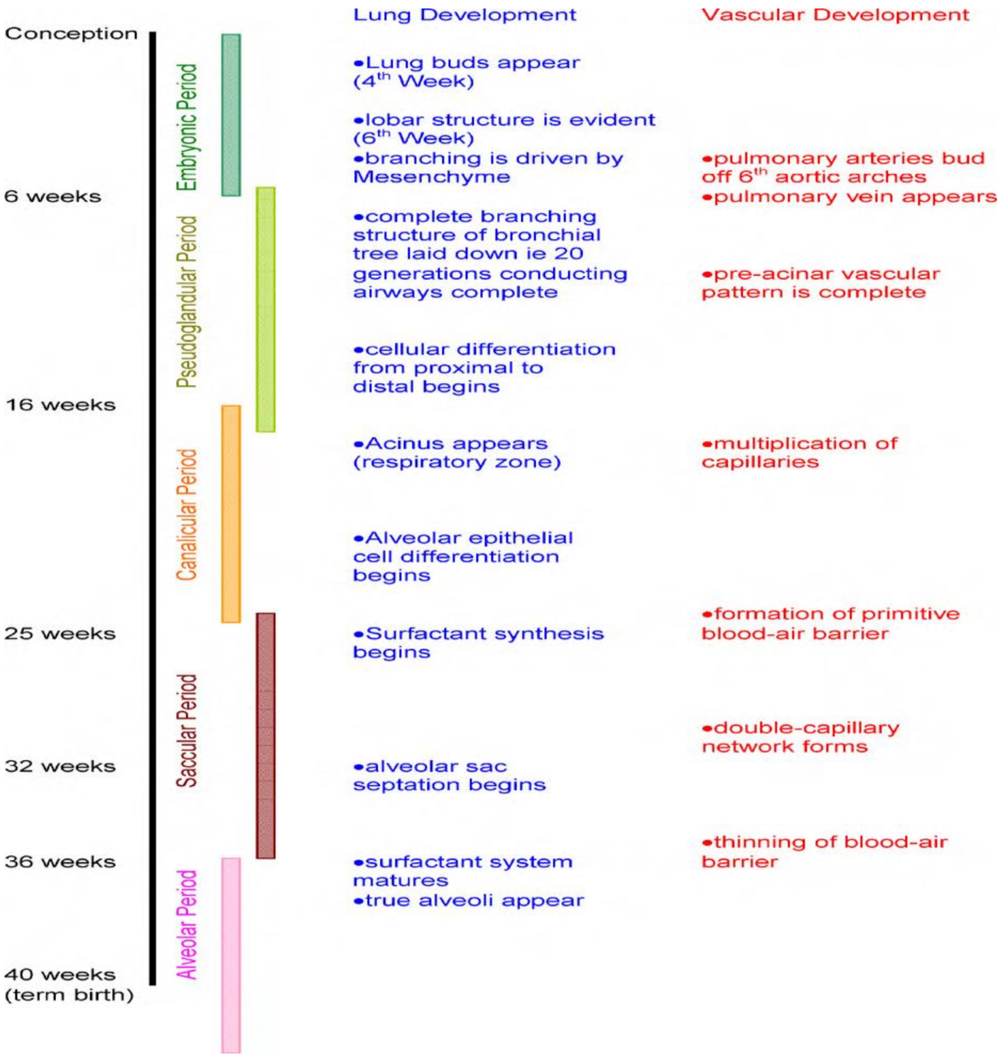


Fig. 2 - The different stages of lung development, from conception to birth. Image adapted from Smith et al. - Normal Development of the Lung and Premature Birth

At birth, the number of alveoli is about 50 million (20% of the number in adulthood), reaching the same number as the adult at 8 years of age, which allows us to consider that the respiratory system of young children is constituted mainly through bronchial conduits (Davis & Mychaliska, 2013). However, a recent study with the inhalation of hyperpolarized helium (He3) contradicts this idea, as it demonstrates that the size of the alveoli does not change between 7 and 21 years of age, but increases in number (Narayanan et al., 2012; Ochs et al., 2004). This reduction in respiratory units (respiratory bronchioles and alveoli) is also accompanied by a lower calibre of the ducts (Zeltner & Burri, 1987). A new-born has terminal bronchioles with a diameter of 0.1 mm, increasing to 0.2 mm at 2 years and 0.3 mm at 4 years. This marked reduction in the gauge leads to a low conductance, leading to a great resistance of the air in the ducts, explaining why a bronchial obstruction during a respiratory pathology in a young child is so severe (Neumann & von Ungern-Sternberg, 2014; Yau et al., 1999). This calibre reduction associated with low thoracic compliance predisposes to the collapse of the distal airways (Postiaux, 2004; Postiaux et al., 2018).

Other important aspects that are reduced or absent in the new-born are the Martin or Lambert channels, which appear at around 6 years of age, and the Kohn pores that form after 6 months of age, but in small quantity (Zeltner & Burri, 1987). These channels and pores allows the collateral ventilation, which does not exist in young children, and, in the event of a bronchial obstruction, fully atelectatic lung areas may appear, as it is not possible to deliver air to the alveoli downstream of the obstruction (Gompelmann et al., 2013; Postiaux, 2004; Postiaux et al., 2018; Terry & Traystman, 2016).

Another important anatomophysiology difference, compared to adults, is a higher density of mucus-secreting cells, and of greater dimension in relation to the bronchial wall and airway diameter (Bustamante-Marin & Ostrowski, 2017; Sleigh et al., 1988). In the case of an inflammation of the bronchial tree, the increased production of secretions associated with the lower calibre of the ducts, the lower thoracic compliance, the hyperinflation physiologic with horizontalization of diaphragm, and the absence of collateral ventilation, leads to severe bronchial obstruction and consequently to breathing difficulty (Postiaux, 2004; Postiaux et al., 2018).

3. BRONCHIOLITIS

3.1 General considerations, epidemiology and diagnosis

Bronchiolitis is one of the main pathologies, if not the main reason for admission to hospital emergencies, in the autumn and winter periods in Portugal and the rest of the world (Bryan et al., 2017; Direção Geral da Saúde, 2012). Its main infectious agent is RSV, which is currently called human RSV (hRSV), with other triggering agents, such as rhinovirus, parainfluenza type 3, metapneumovirus, adenovirus and mycoplasma pneumoniae as less frequent (Afonso et al., 2016; Schaap-Nutt et al., 2012; Smyth, 2007; Soto et al., 2020; Van Ginderdeuren et al., 2017). The diagnosis of bronchiolitis is made, above all, by the patient's history and physical assessment, and the degree of severity must be established by the risk factors that may be associated (Direção Geral da Saúde, 2012; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Silver & Nazif, 2019). Prematurity (especially preterm infants less than 29 weeks of gestation) who miss the period of placental antibody transfer, age less than 6 months, congenital cardio pneumopathies, metabolic diseases, myopathies, trisomy 21, cerebral palsy and passive exposure to tobacco smoke are factors that contribute to the increased severity of bronchiolitis (Merianos et al., 2017; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Silver & Nazif, 2019).

The routine use of chest X-rays or laboratory tests are not recommended by national nor international guidelines (Direção Geral da Saúde, 2012; Excellence, 2016; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Society, 2018). Laboratory tests conducted to search for viral agents and routine radiological examinations are not recommended because they do not help in the diagnosis or will change the treatment plan and may could lead to an increase in the prescription of antibiotics (Direção Geral da Saúde, 2012; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Silver & Nazif, 2019).

This pathology presents, usually with a rhinorrhoea, cough, tachypnoea, signs of circulation and crackles on auscultation (Baraldi et al., 2014; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Silver & Nazif, 2019). The child's parents or caregivers often report decreased food intake and episodes of vomiting, which can lead to dehydration, especially in children under 6 months of age. In the most severe cases, oxygen levels drop significantly and children may have SpO_2 below 90%, requiring supplementary O_2 administration through a nasal mask or cannula (Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014).

Continuous monitoring of SpO_2 is not recommended, except in severe cases, as it is known that throughout the day and night it is normal for the child to have large fluctuations in blood O_2 levels (Cunningham, 2015; Principi et al., 2016). Continuous monitoring leads to increased time of O_2 supplementation and longer hospital stay (Hendaus et al., 2015; Quinonez et al., 2017; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014). O_2 supplementation should only be done if the child has SpO_2 values below 90%, and should be stopped when the child starts to have saturations above 95% (Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014).

The percentage of hospitalization is between 1% and 3%, of which only about 1% needs intensive care (Green et al., 2016; Mendes-da-Silva et al., 2019).

3.2 Pathogenesis

The main infectious agent of bronchiolitis is RSV, triggering a combination of several situations, such as oedema of the airways, increased production of secretions and necrosis of the bronchial epithelium, as a result of cytotoxic lesions (Rossi & Colin, 2017; Silver & Nazif, 2019; Soto et al., 2020). Viral replication begins in the nasal mucosa, causing an exuberant immune response, with an influx of immune cells, lymphocytes and granulocytes in the epithelium (Smyth, 2007). After an incubation period of 4 to 6 days, the first symptoms appear in the upper airways, such as nasal obstruction and rhinorrhoea (Silver & Nazif, 2019). Approximately one third of the upper airway infections migrate to the lower airways (bronchial tree), causing a narrowing of the bronchial lumen and a consequent increase in duct resistance (decreased conductance) (Silver & Nazif, 2019; Smyth, 2007). The narrowing or total occlusion of the distal airways causes hyperinflation and atelectasis in several pulmonary zones, which may decrease the ventilation / alveolar perfusion ratio, leading to increased respiratory effort and hypoxemia (Barreira et al., 2011; Silver & Nazif, 2019). As a consequence of the inflammation, a fibrosis process develops, which can be distributed in nodules or in a diffuse way, which may involve the peribronchiolar alveoli and be one of the causes of the narrowing of the distal airways (Colby, 1998; Rossi & Colin, 2017). This may explain the great variability of radiological findings, such as nodules, branched lines, air trapping, mosaic perfusion, ground-glass imaging and a mixture of these situations, which makes it difficult to diagnose bronchiolitis based on a lung radiography (Colby, 1998; Muller & Miller, 1995). This is one of the reasons why the use of radiological exam in bronchiolitis is not recommended.

The clinical aspects, after infection of the lower airways, include coughing, wheezing, tachypnoea, and signs of increased respiratory effort which, in the most severe cases, include intercostal, subcostal and / or supraclavicular retractions, nasal flaring, hyperextension of the head with pumping movements and grunting (Silver & Nazif, 2019). The evolution of bronchiolitis is very variable and dynamic, constantly changing. Usually, it presents a period of more severe symptoms, on the third or fourth day of the disease (Kyler & McCulloh, 2018; Swingler et al., 2000). Even during an assessment, for example in a hospital emergency, the findings in the assessment can change in a short period of time, requiring repeated evaluations to establish a more accurate diagnosis (Silver & Nazif, 2019).

After the acute period, the recovery phase may take 13 to 17 weeks for the epithelial tissue to recover entirety, maintaining a large percentage of destroyed cilia cells (approximately 58%) after 6 weeks (Wong et al., 2005).

3.3 Instruments for severity assessment

Due to the complexity and constant variability of the clinical status and severity of a child with bronchiolitis, several respiratory scores were created to help clinicians to establish the degree of severity, and help in the management decision, when evaluating a child in a hospital emergency room. These scores are also used as an assessment tool in clinical studies, to investigate the effect of a particular medication, device or treatment technique on bronchiolitis.

Initially, asthma assessment scores were adapted to evaluate severity in children with bronchiolitis, but as they did not have a good reliability for predicting the severity of bronchiolitis, researchers developed different specific scores. The first score date from the mid-1960s but since then several others were developed (Rodriguez-Martinez et al., 2018).

Variability among scores is enormous. While some scores use a large number of evaluation parameters [e.g.: Children's Hospital of Wisconsin Respiratory Score (CHWRS)], others use only 4 or 5 parameters [e.g.: Wang Respiratory Score (WRS); Kristjansson Respiratory Score (KRS)], and require the use of medical devices (e.g.: oximeter; stethoscope). The vast majority use common parameters, such as respiratory rate (RR), heart rate (HR), SpO_2, chest retractions, dermal colour change (cyanosis) and the child's general condition such as changes in food intake, sleep disturbance or signs of irritability (Rodriguez-Martinez et al., 2018).

When considering which score to use in an emergency room, to help in the decision to intern or refer to home, or as an assessment tool in a clinical study, several aspects should be taken into account, such as its reliability and validity (Mokkink et al., 2010).

Scores such as Tal Score (Tal et al., 1983), the Modified Tal Score (MTS) (McCallum et al., 2013), the Respiratory Distress Assessment Instrument (RDAI) (Lowell et al., 1987), the Respiratory Score of Liu (RSL) (Liu et al., 2004), the CHWRS, the Respiratory Distress Score (RDS) (Can et al., 1998), the Respiratory Index Score (RIS) (Chong et al., 2017), the Bronchiolitis Risk of Admission Score (BRAS) (Marlais et al., 2011), the WRS and the KRS are examples of instruments designed for bronchiolitis and used in clinical studies of this pathology. Eight of the scores have common items, such as RR, wheezing and chest retractions. The differences between the scores are the addition or absence of other items (e.g.: mental state; general condition; SpO_2; dermal colour; HR) and the points assigned to each item, which can vary from zero to four values per item.

The analysis and comparison of these scores led us to the conclusion that the vast majority of them lack validation. RIS reports good sensitivity and moderate specificity (Chong et al., 2017), while RSL refers only moderate inter-observer reliability (Liu et al., 2004). The RDS and BRAS (specifically created for use in the emergency room and to help with the decision to stay), have not been validated or analysed for their reliability (Can et al., 1998; Marlais et al., 2011). Only four scores have a validation, together with the analysis of inter-rater and intra-rater reliability, namely, the RDAI, CHWRS, WRS and KRS. The RDAI and CHWRS (Destino et al., 2012; Fernandes et al., 2015) present low construct validity and low and modest inter-rater reliability, respectively. WRS and KRS present a moderate criterion validity with good inter-rater reliability (Chin & Seng, 2004; Pinto et al., 2020).

3.4 Treatment

In several countries, guidelines have been developed to guide clinicians in the management of bronchiolitis (Excellence, 2016; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Society, 2018). In Portugal, the first national guideline was developed in 2012, by the General Directorate of Health (Direção Geral da Saúde, 2012). These management recommendations cover diagnosis, complementary tests, supportive measures, and medication that may be administered in the emergency department.

According to the guidelines, the treatment of bronchiolitis is mainly supportive (Direção Geral da Saúde, 2012; Excellence, 2016; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Society, 2018). It is essential to normalize the levels of hydration and O_2, and the food supply. Increasing the number of meals and each meal with less amount of food, or administering fluids by nasogastric tube or by intravenous route, in the most severe cases, are some of the recommended measures to maintain the hydration status of the child. Other support measure consists of nasal clearance by gentle nasal aspiration (Direção Geral da Saúde, 2012; Excellence, 2016).

Inhaled bronchodilators, inhaled corticosteroids, antiviral therapy, antibiotics (unless bacterial co-infection is proven) and respiratory physiotherapy (Direção Geral da Saúde, 2012; Perrotta et al., 2005, 2007; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Roque i Figuls et al., 2012; Roque i Figuls et al., 2016) are not routinely recommended. However, adherence to these recommendations is far from perfect, and is widely contested in clinical practice (Fontoura-Matias et al., 2020; Kirolos et al., 2019).

In some guidelines, the use of bronchodilators in the emergency room, if a therapeutic test performed in this setting showed an improvement in the child's clinical condition, was still proposed (Direção Geral da Saúde, 2012) but, in recent years, even this is not a matter of debate and guidelines are being reviewed because meta-analysis of clinical trials on the administration of bronchodilators in the treatment of bronchiolitis do not show a clinical significant improvement, in hospitalized or outpatient patients. Bronchodilators do not reduce the rate of hospital stay after outpatient treatment, do not decrease the length of stay, and do not decrease the time to resolve the disease in outpatient studies (Gadomski & Scribani, 2014). One of the reasons that could explain this lack of response to bronchodilators in children up to 2 years of age, is the deficiency of pulmonary beta-agonist receptors and immature bronchiolar smooth muscle (Cai et al., 2020) which, when relaxed by the action of the bronchodilator, becomes hypotonic, ceasing the action as a stabilizer of the bronchial walls, leading to the collapse of the distal airways (Olsen et al., 1967; Sparrow & Lamb, 2003).

On the benefit of administering nebulized epinephrine in the context of urgency and hospitalization, studies prior to 2012 show an improvement in the child's clinical condition (Langley et al., 2005). However, more recent studies show that there is no benefit in administering this type of medication, either alone or associated with corticosteroids (Kua & Lee, 2017).

Nebulization with hypertonic serum is another form of treatment to improve the clearance of excess secretions, the main cause of bronchial obstruction, which consequently leads to the appearance of atelectatic lung zones, and lead to ventilatory difficulties and desaturation. Hypertonic serum has been shown to increase mucociliar clearance levels in normal individuals and in patients with asthma, bronchiectasis, cystic fibrosis and sinonasal diseases (Kellett et al., 2005; Zhang et al., 2017). Such benefits would also be expected in infants with bronchiolitis (Mandelberg et al., 2003; Zhang et al., 2017). However, more recent studies and systematic reviews contradict this indication, as clinical trials did not demonstrate benefits in the use of hypertonic serum in bronchiolitis (Harrison et al., 2018; Heikkila & Korppi, 2016). It should be noted that these results were obtained in clinical trials in hospitalized patients, trying to find out if the hypertonic serum reduced the length of stay.

Focus should be put in the implementation of preventive measures to avoid dissemination of the infection, such as disinfection of hands with antimicrobial or alcohol-based solution, before and after any direct contact with the child, isolation from contact with other children and avoid child exposure to tobacco smoke (Direção Geral da Saúde, 2012; Merianos et al., 2017; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014). Studies on passive exposure to tobacco smoke show that children have a significant decrease in lung function, greater severity of the disease (e.g.: bronchiolitis, asthma or pneumonia) and an increase in the use of resources (e.g.: hospitalization) compared to children not exposed (Merianos et al., 2017).

Despite the little evidence, demonstrated in studies and systematic reviews, of the benefits of chest physiotherapy, it is thought that its introduction into the bronchiolitis treatment protocol would be beneficial.

4. ROLE OF CHEST PHYSIOTHERAPY IN BRONCHIOLITIS MANAGEMENT

Chest physiotherapy, alone or associated with the administration of nebulized saline and/or mucolytics, has been used for several decades as a complementary treatment for clearing the upper and lower airways. It was in the 50s of the XX century that chest physiotherapy started to be applied regularly in patients with bronchial obstruction, due to the accumulation of secretions, in adults or children with cystic fibrosis (McIlwaine, 2007). The techniques developed to help the natural mucociliar drainage of the human body were postural drainage, percussion (clapping), vibration, autogenic drainage and directed coughing / huffing (Mackenzie et al., 1980; McIlwaine, 2007). Postural drainage consists of placing the patient upside down in different positions so that the action of gravity moves the secretions from the peripheral to the proximal airways. Simultaneously, percussion is applied on chest to detach the secretions from the bronchial walls. After a period of 3-5 minutes of percussion, several deep breathing cycles are requested and manual vibration is applied over the chest to move the secretions through the bronchi. When secretions reach the proximal pathways, a directed coughing or huffing is requested (maximum expiration, after a maximum inspiration, within one second) (Matthews et al., 1964; Van der Schans, 2007). Typically, the time taken for a classic chest physiotherapy session is 50 to 60 minutes (Mackenzie et al., 1980).

In bronchiolitis, the accumulation of secretions and obstruction of the upper and lower airways is a constant problem, leading to situations of atelectasis and / or decreased pulmonary ventilation (Postiaux, 2004; Postiaux et al., 2011). To solve this problem, physiotherapy, especially in Anglo-Saxon countries, adapted the bronchial clearance and cleaning techniques used in cystic fibrosis and in adults with bronchial obstruction, the classical chest physiotherapy (Nicholas et al., 1999; Postiaux, 2004; Webb et al., 1985). In the last decade of the XX century, in France, a new technique to remove secretions from the bronchial tree has emerged (Gajdos et al., 2010). This technique consists of an expiratory flow acceleration (EFA), through a quick compression of the chest and abdomen (Gajdos et al., 2010). Efficiency is reduced, especially in the most distal airways, as it causes collapse of the airways and on rare occasions rib fracture (Chalumeau et al., 2002; Gajdos et al., 2010).

The techniques described above, such as postural drainage, percussion, vibration and EFA, seem to make sense to help detach and move secretions through the bronchial tree and eliminate them through cough. Several randomized studies have been carried out to understand the effectiveness and contribution of these techniques in improving children with bronchiolitis. All studies were carried out in the context of hospitalization, seeking to establish whether there was a reduction in hospital stay and an improvement in the values of respiratory scores. However, the results did not show a reduction in hospital stay or improvement in the children's respiratory severity (Gajdos et al., 2010; Nicholas et al., 1999; Perrotta et al., 2005, 2007; Roque i Figuls et al., 2012; Roque i Figuls et al., 2016; Webb et al., 1985).

As there is no evidence of the effectiveness of chest physiotherapy in bronchiolitis, the guidelines created internationally state that chest physiotherapy should not be used (Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014). Since 2006, year of publication of the American Academy of Paediatrics (AAP) Guidelines, that all the systematic reviews on the use of chest physiotherapy in bronchiolitis mention that there is no advantage in its use (Perrotta et al., 2005, 2007; Roque i Figuls et al., 2012). The exception appears in the last Cochrane review (Roque i Figuls et al., 2016), which refers to studies using techniques such as Prolonged Slow Expiration (PSE) and Provoked Cough (PC), which had a positive impact in reducing the respiratory score and decreasing bronchial obstruction (Gomes et al., 2012; Postiaux et al., 2011; Rochat et al., 2012; Roque i Figuls et al., 2016). In 2019, a randomized study of children hospitalized with bronchiolitis reports that the group that performed chest physiotherapy with PSE had a significant improvement in the values of the respiratory severity score (Conesa-Segura et al., 2019).

4.1 Prolonged Slow Expiration

PSE is a technique based on the child's anatomophysiology up to 2 years old, and is not an adaptation of techniques used in adults or children with cystic fibrosis. The reason is that a child up to 2 years of age does not have the fully developed bronchial tree, or structures as the Martin or Lambert channels and Kohn pores (Gompelmann et al., 2013; Terry & Traystman, 2016; Zeltner & Burri, 1987). The reason is that a child up to 2 years of age does not have the fully developed bronchial tree, or structures as the Martin or Lambert channels and Kohn pores (Gompelmann et al., 2013; Postiaux, 2004; Postiaux et al., 2018). As a result, in case of obstruction of a bronchus, the pulmonary lobe is no longer ventilated, leading to atelectasis, increased respiratory effort and consequent desaturation and respiratory failure (Silver & Nazif, 2019; Smyth, 2007). The PSE was developed with the following aspects in mind: the absence of compensatory mechanisms for an obstruction and the acceleration of the air within the peripheral airways that easily leads to its collapse (Fig.3) (Postiaux, 2004; Postiaux et al., 2011; Postiaux et al., 2018; Sparrow & Lamb, 2003).

PSE is achieved through simultaneous manual pressure of the chest and abdomen (Fig. 6), which starts at the end of the child's expiratory phase, taking the lungs to the residual volume and maintaining this position for 3 breathing cycles (Postiaux, 2004; Postiaux et al., 2011).

Fig. 3 - Positioning of hands to perform the PSE. Image taken from the site https://pdfs.semanticscholar.org/6ab5/022aafa511fb93d8d8e46e894e1b318b2868.pdf

This procedure allows triggering an increase in the inspiratory volume (sigh), through the Hering-Breuer reflex (Lanza et al., 2011; Rabbette & Stocks, 1998). We can perform this manoeuvre in 4 or 5 consecutive exhalations, and assess whether there has been a displacement of secretions that trigger the cough or if it is necessary to provoke it. The manoeuvres end when it is noticed that there are no secretions in the bronchial tree or if the child shows signs of tiredness. This assessment and decision-making are carried out through pulmonary auscultation and analysis of the sounds captured, and observation of the child's general condition (see title 4.4 - Chest physiotherapy assessment) (Postiaux, 2004). All treatment is done with the child in supine position, on a stable and slightly padded surface. There is no need to use other decubitus, as children up to 2 years of age do not have decubitus dependence, due to the lack of collateral ventilation and the distal airways are not so far from the trachea. For the same reasons, there is also no need to use inclined planes, and because it is known that gravity (by itself) has no effect on the displacement of secretions (Postiaux, 2004; Postiaux et al., 2018).

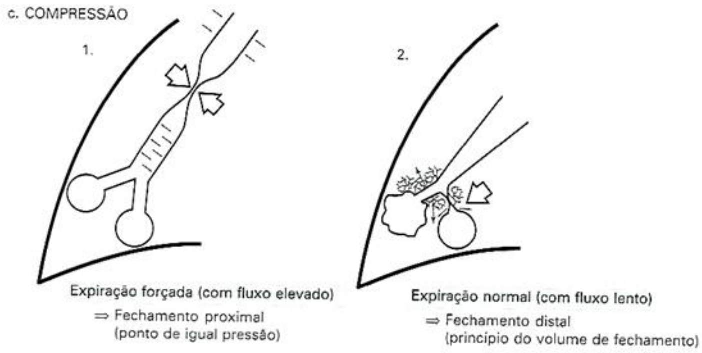
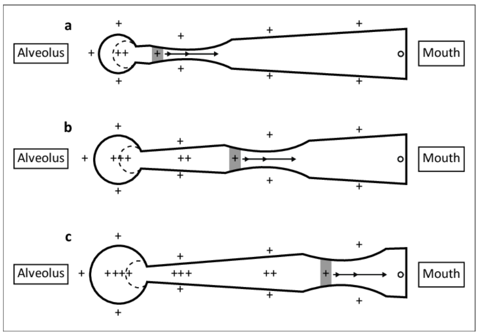


Fig. 4 - Demonstration of the effect of accelerating expiratory flow, compared to slow flow. Image adapted from the book “Paediatric respiratory physiotherapy - Treatment guided by pulmonary auscultation” by Guy Postiaux

To better comprehend this mechanism, it is important to understand the concept of point of equal pressure (PEP), which occurs naturally in a healthy individual, when it triggers cough or increases the expiratory flow, leaving only the residual volume inside the lungs (expiration until the end of vital capacity). PEP is the point where the intrabronchial pressure equals the pressure external to the air conduit (pleural pressure - P_{pl}) (Mead et al., 1967; Pedersen & Butler, 2011; Postiaux, 2004; Postiaux et al., 2018; Voets & van Helvoort, 2013; Zach, 2000). This point moves from the trachea to the peripheral airways (bronchioles) as the lung volume decreases (Fig. 4), with an increase in intrabronchial pressure in the PEP-Alveolus section, this section is dilated, compared to the section upstream of the PEP (Fig. 5) (Mead et al., 1967; Zach, 2000).

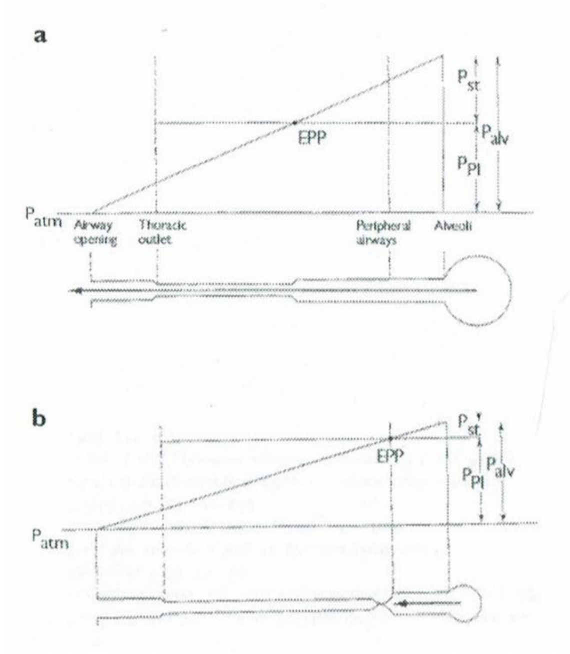
If associated with this principle, there is an obstruction due to the accumulation of



secretions, the resistance to flow will increase and the pressure will drop abruptly, causing the collapse of the airway (Voets & van Helvoort, 2013). Also contributing to the collapse of bronchioles is the lack of a cartilaginous structure that counteracts P_{pl} (Fig.5) (Mead et al., 1967; Pedersen & Butler, 2011).

Fig. 5 - Location of the PIP in different volumes, (a) low volume, (b) medium volume and (c) high volume. Image adapted from the site https://www.researchgate.net/figure/The-equal-pressure-point-during-a-forced-expiratory-technique-at-different-lung-volumes_fig4_334032335

Another important anatomophysiology aspect of small children is their greater pulmonary



compliance (more elastic rib cage), which is more easily deformable (compressed), allowing an easier collapse of the airways (Hopkins & Sharma, 2020; Zach, 2000). Thus, it is clear why PSE is performed slowly, as this way we do not cause the collapse of the peripheral airways and create an intrabronchial pressure differential, from the periphery to the proximal pathways, which helps in the movement of secretions in the same direction (Postiaux, 2004; Postiaux et al., 2011; Postiaux et al., 2018; Postiaux et al., 2013).

Fig 6 - PEP position depending on the change in alveolar pressure. Image adapted from the article "The physiology of forced expiration" of M.S. Zach

Secretions reaching the first bronchial branches can be eliminated through spontaneous or provoked cough. The elimination of more proximal secretions will promote changes in the rheological properties in the secretions that will be produced *a posteriori* (Sleigh et al., 1988). These new secretions will have a viscoelastic composition, which will allow a more effective action of the cilia, increasing the mechanisms of mucociliar cleaning.

Thus, secretions from the distal airways may migrate to the proximal pathways, being eliminated from the lungs (Cohen, 2006).

4.2 Retrograde Rhinopharyngeal Clearance

Anatomically, the human nasal cavities are designed so that the secretions produced in the nasal mucosa drain in the posterior direction, directly to the nasopharynx / oropharynx, where they will be swallowed and eliminated by the digestive system (Sahin-Yilmaz & Naclerio, 2011). During a bronchiolitis, one of the symptoms that is always present is an increase in the production of secretions, initially in the upper airways, causing a total or partial obstruction of the nasal cavities (Silver & Nazif, 2019). This situation leads to an increase in respiratory effort, especially in children under 6 months of age, since at these ages they breathe predominantly through the nasal route (Postiaux, 2004; Postiaux et al., 2018; Smith & Ishman, 2018). When this does not happen, the child has great difficulty in feeding or is unable to do so at all, which implies a decrease in their quality of life (Smith & Ishman, 2018). The new-born with bilateral nasal obstruction may show signs of desaturation (cyanosis; circulation; dyspnoea), as he is unable to coordinate swallowing (feeding) and breathing. If left untreated, it can result in decreased development (Smith & Ishman, 2018).

In a hospital context, in emergency or inpatient rooms, the established norm for clearing the nasal cavities is mechanical suction (Guideline, 2004). This procedure uses a central negative pressure system and a flexible probe, which is inserted alternately in the nasal cavities up to the oropharynx. This level is very often exceeded and gastric contents are suctioned. It can be seen that this procedure easily traumatizes the nasal mucosa, causing small haemorrhages, being extremely uncomfortable for the child (Guideline, 2004).

In the domestic context, oral aspiration is the most accessible, being done by the parent/guardian, through suction in a device. This procedure seeks to obtain negative pressure in the device, which is introduced at the entrance of the nasal cavities. The effectiveness is very low and the objective of unclogging / cleaning the nasal cavities is not achieved. The ineffectiveness is explained by the anatomophysiology of the human nasal cavities, which are developed so that the vast majority of secretions produced in the nasal cavities, drain into the pharynx. Only the inferior nasal turbinate drains anteriorly to the entrance of the nasal cavities (Sahin-Yilmaz & Naclerio, 2011).

Because there is an urgent need to unblock the upper airways and keep them permeable, chest physiotherapy has developed a technique that does not use any type of device and takes into account the anatomy of the child with a few months old (Gomes, 2016). Called retrograde rhinopharyngeal clearance (RRC), this technique consists of instilling a few drops of saline or sprayed seawater into the nasal passages, followed by closure of the mouth cavity at the beginning of the inspiratory phase. This forces the child to inhale through the nasal cavities, displacing the serum and secretions, which are found there, to the oropharynx (Alexandrino et al., 2017; Gomes, 2016; Postiaux, 2004). This usually causes coughing and consequent swallowing of the secretions. In this way it is possible to eliminate secretions from the nasal fossae in a more effective way and without causing trauma to the mucosa (Alexandrino et al., 2017; Gomes, 2016). This technique is simple, effective, with reduced adverse effects, which is an excellent tool to be taught to caregivers of children with nasal obstruction (Alexandrino et al., 2017). At first, caregivers are apprehensive about the manoeuvre but after doing it once or twice, they quickly realize its effectiveness and absence of adverse effects, becoming a common practice whenever the child has upper airway obstruction due to accumulation of secretions.

4.3 Provoked Cough

Coughing is a physiological mechanism to eliminate pulmonary secretions, sending them to the digestive system. Is triggered off when secretions reach the trachea and stimulate the cough reflex, which is located on its wall (Banner, 1986). When the cough reflex does not occur spontaneously, it can be provoked by putting pressure on the trachea, just above the upper edge of the sternal manubrium (Fig. 7).

Fig. 7 - Tracheal pressure point to provoke the cough reflex. Image taken from the site https://www.postiaux.com/pt/metodo/technicas.html

This technique is possible in young children, with relative safety because, up to 2 years old, they present the trachea in an extra thoracic position (Postiaux, 2004; Wadie, 2012). At birth, the new-born's larynx is high in relation to the cervical spine. The upper edge of the larynx is at the level of the space between the body of the 3rd and 4th cervical vertebrae, very close to the base of the head (Postiaux, 2004; Wadie, 2012). Another aspect is the structural maturation of the cartilaginous rings of the trachea. These show great complacency, easily deformable when pressure is placed on the trachea (Banner, 1986; Postiaux, 2004; Postiaux et al., 2011). This aspect, associated with the superior location of the trachea, allows to putting pressure on it, stimulating the cough reflex, without causing structural damage.

4.4 Chest physiotherapy assessment

Accurate evaluation is essential in chest physiotherapy. Through careful evaluation, it is possible to know whether the child's respiratory stress has increased or decreased, whether secretions have progressed from the most distal pathways to larger-calibre pathways and whether the techniques are being effective (Postiaux, 2004; Postiaux et al., 2011).

In order to decide which techniques to use and when the treatment should be concluded, the physiotherapist makes an assessment of the clinical status, through the present and past clinical history, by observing signs of respiratory difficulty (increased RR; chest retractions; nasal flapping; cyanosis) and pulmonary auscultation (Fig. 8).

Auscultation is essential for making a correct decision. Through auscultation, the physiotherapist is able to find out if the child has upper and lower airway obstruction. Snoring or crackling sounds exclusively in the nasal cavities, indicates that the child has only obstructed upper airways, being necessary to purify the nasal cavities through RRC. If auscultation of the rib cage presents wheezing and / or crackling sounds, it is a sign of the presence of secretions in the lower airways. The exclusive presence of wheezing is not indicative of bronchospasm, but of a decrease in bronchial calibre in a given area. In bronchiolitis, the decrease in bronchial calibre is caused by oedema of the mucosa and accumulation of secretions adhering to the bronchial walls. In an early stage of bronchiolitis, we can only have oedema of the mucosa, hearing only wheezing, which does not disappear after the application of PSE, because this technique only has an effect on secretions (Sanchez Bayle et al., 2012). However, when wheezing subsides and crackles appear after PSE, it is a sign that the secretions adherent to the bronchial walls, loosened and moved to larger calibre pathways (Postiaux, 2004; Postiaux et al., 2018). In children older than 6 months, the inspiratory and expiratory phase can be divided into 3 parts (prophase / mesophase / telophase), allowing to know if the secretions are in the proximal, distal or peripheral bronchi. As the crackles are audible in the prophase, we know that the secretions are found in the proximal pathways, making it possible to provoke the cough and eliminate them (Postiaux, 2004; Postiaux et al., 2018; Postiaux et al., 2013).

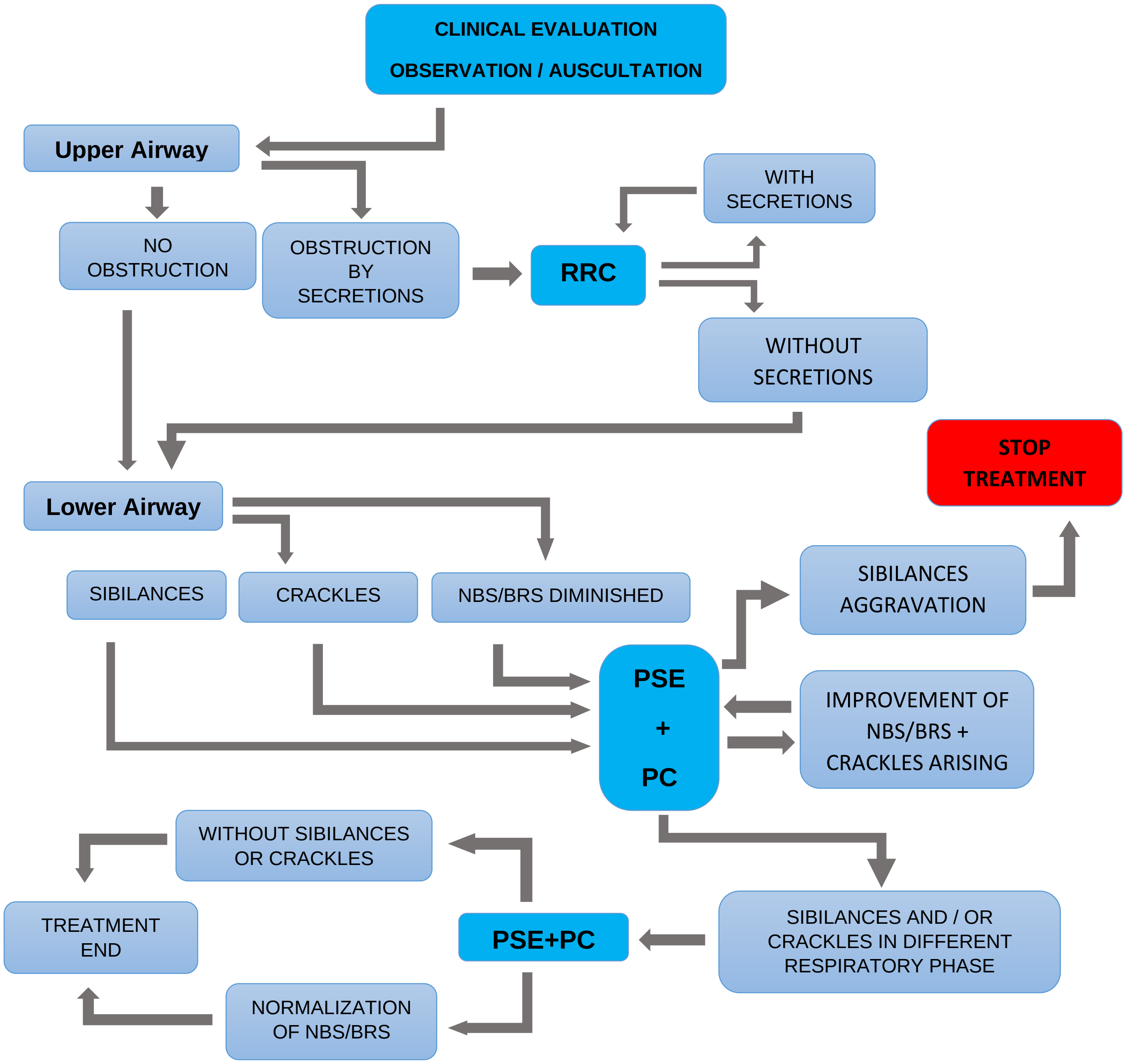


Fig. 8 - Flowchart of intervention for clearing the upper and lower airways. Based on the decision-making scheme proposed by Guy Postiaux (Postiaux, 2004).

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CHAPTER 2 – STUDY 1

Comparison of Kristjansson respiratory score and Wang respiratory score in infants with bronchiolitis in a hospital emergency department

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Comparison of Kristjansson Respiratory Score and Wang Respiratory Score in infants with bronchiolitis in a hospital emergency department

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Objectives: Several respiratory scores have been created to evaluate bronchiolitis' severity level, but it is still not clear which is the best score. The aim of this study is to compare the Wang Respiratory Score (WRS) and the Kristjansson Respiratory Score (KRS) in the setting of an emergency room.

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Methods: We performed a prospective observational study with 60 infants with bronchiolitis admitted to a paediatric emergency department. For both scores, we assessed inter-rater reliability between two different health professionals (physician and physiotherapist), internal consistency, and correlation with SpO_2 testing the intraclass-correlation coefficient (ICC), weighted kappa, Cronbach α coefficient and Spearman tests, respectively.
Results: The inter-rater reliability was higher in KRS (ICC 0.79) and the Cronbach α and weighted kappa had similar values in KRS versus WRS. The correlation between the KRS/WRS and SpO_2 was poor/moderate upon admission and discharge for the first observer and the second observer.
Conclusions: While the internal consistency was similar in both scores, inter-rater reliability of KRS was higher than WRS, which allows us to conclude that it would have more consistent results when used to assess bronchiolitis' level of severity by health personnel in a busy hospital emergency room.

Keywords: Bronchiolitis; infants; symptom assessment; severity score.

Introduction and Objectives

Acute bronchiolitis, an inflammation of the lower respiratory tract, is one of the most common respiratory diseases affecting infants and it imposes an enormous burden on healthcare resources worldwide.[1] In most cases, however, it is a self-limited condition and one that can be treated at home.[1–3] In fact, only 1–3% of children need to be hospitalized.[4,5] Aspects such as clinical history, respiratory parameters, risk factors and oxygen saturation levels, are used by physicians in emergency departments to distinguish between a mild, moderate or severe case of bronchiolitis, in order to decide if hospitalization is necessary.[3]

An accurate assessment of the level of severity is thus crucial in the case of bronchiolitis for two main reasons: (a) to decide on the need for close monitoring and hospitalization; and (b) for research purposes, to allow comparisons between study groups. Several respiratory scores have been created to assess the level of severity and progression of the disease as well as the efficacy of therapeutic interventions. Examples of such scores are the Tal Score,[6] the Modified Tal Score (MTS),[7] the Respiratory Distress Assessment Instrument (RDAI),[8] the Wang Respiratory Score (WRS)[9] and the Kristjansson Respiratory Score (KRS).[10] Most of these scores use the main clinical signs of bronchiolitis for assessment of severity level, not being clear which is the best score and which should be used in a given setting.

Currently, the RDAI is the score most commonly used by physicians in a clinical trial setting, but although it has adequate inter-rater reliability, the construct validity ranges from poor to moderate. In addition, its use by health professionals can be challenging,[11] as it is difficult to evaluate the presence of wheezing throughout the respiratory cycle at high respiratory rates.

In the context of this study, we have decided to examine WRS[9] and KRS,[10] scores specifically developed to assess bronchiolitis' severity level. The motivations behind this choice were threefold: (a) the acknowledged need for a score easy to use in a hospital emergency by health professionals other than physicians; (b) the advantage of being easy to apply in emergency departments; and (c) the fact that these scores had been designed on the basis of specific physical parameters common in children with acute lower airway infections, such respiratory frequency, chest recessions and wheezing.[12,13]

Both scores are very similar in terms of the parameters they include (the difference being that KRS additionally includes 'skin color'), and had never been studied/used by different health professions. Chin and Seng[14] study was the first which compared these two scores, but included only physicians. The purpose of this study is to compare WRS and Kristjansson Score and establish the inter-rater reliability and internal consistency when used by physicians and a physiotherapist.

Materials and Methods

Study design and population

This was a prospective observational study in a convenience sample of Portuguese infants admitted with acute bronchiolitis. Data were collected between January and May of 2010, in the paediatric emergency department of the Centro Hospitalar Universitário São João, Porto (CHUSJ), a tertiary care hospital. Inclusion criteria were: all children aged less than 24 months diagnosed with bronchiolitis by a physician from one of two different emergency teams working on Monday and Wednesday (from 4 p.m. to 2 a.m.) or Saturday and Sunday (from 9 a.m. to 2 a.m.) in weekend. Children with history of prematurity, underlying cardiopulmonary disease or immunodeficiency were not excluded from the study, since the aim of this study was to evaluate the performance of respiratory scores in defining the level of respiratory distress, regardless of the presence of risk factors. Exclusion criterions were as follows: all children with severe hypoxemia, needing oxygen supplementation or needing invasive or non-invasive ventilation. These are all criteria for inpatients with bronchiolitis and thus not compatible with this study focused on outpatients only.

Assessment

Two observers (one physician and one physiotherapist) independently assessed all children using both WRS (Table A.5) and KRS (Table A.6) in the paediatric emergency department. This was completed upon admission and discharge within a time frame of approximately 15 min between observations. The first assessment was always made by the physician, being the physiotherapist the second before the medical treatment starts. Before the start of the study, all observers were briefed on the purpose of the study and how to fill in each respiratory score. The first observer (from a group of 24) was a physician, a paediatrician or a resident in paediatrics, and the second observer was one physiotherapist, the main investigator. The physician's years of experience were not taken into account and their inter-rater reliability was based in the Chin and Seng[14] study, when distributing the cases in the emergency department and each observer was blinded to the other observer's assessment. The children were evaluated in a calm environment, while awake and not crying.

The WRS is a 4-item score which includes respiratory rate, wheezing, chest retraction and general condition. Each clinical sign is scored from zero to three except for the general condition, which is scored zero for normal, or three for irritability or lethargy. The total score ranges from 0 to 12.[9] The KRS is a 5-item score which includes respiratory rate, chest recessions/retractions, breath sound/wheezing, skin color and general condition. Each clinical sign is scored from zero to two and the total score ranges from 0 to 10.[10] Both scores establish severity as the total score increases.

The respiratory rate was determined by counting the number of breath cycles during 60 s. Chest recessions/retractions, skin color and general condition were assessed by observation and breath sounds/wheezing with a stethoscope.

The SpO_2 was recorded in all children, while breathing room-air, with a pulse-oximeter (Dinamap DPC301N-PR, GE Medical Systems Information Technologies, Inc. Milwaukee, USA). The maximum SpO_2 was determined both upon admission and discharge, after the pulse-oximeter had been branched for at least two minutes. If the SpO_2 was below 92%, supplemental oxygen was provided to the patient.

For each patient, additional baseline data were collected, including demographic data, personal and family past medical history. This comprised of medical diagnosed food allergies, rhinitis, asthma and atopic dermatitis, exposure to tobacco smoke, contact with other children, parents schooling level, and medication administered in the emergency department, including supplemental oxygen.

This study was approved by the Ethics Committee of the CHUSJ, Porto. It also complied with the Helsinki Declaration and the current national legislation. Verbal and written consent was obtained from caregivers on behalf of all children enrolled in this study.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 23.0. A Kolmogorov–Smirnov normality test was used and a p value of $p = 0.002$ suggested strong non-normality, leading us to the use non-parametric tests to analyze the data. Skewed variables are presented as median and 25th and 75th percentiles. Differences between groups were evaluated using Mann–Whitney tests, for continuous variables, or Chi-square tests, for categorical variables. The internal consistency of scores items was evaluated by calculating the Cronbach α coefficient; values above 0.70 were considered to represent a good internal consistency.[15,16] Inter-rater reliability of the scores between the first and the second observer were determined using weighted kappa for ordinal variables and intra-class-correlation coefficient (ICC) for continuous variables, on mean-rating $(k = 2)$, one-way random-effects model.[17,18] Power of ICC was established *post hoc*. The idea of using weighted kappa is that disagreements involving distant values are weighted more heavily than disagreements involving more similar values. Agreement was considered to be almost perfect if k was greater than 0.80, substantial if within the range 0.61–0.80, moderate if within the range 0.41–0.60, fair if within the range 0.21–0.40, and slight if below 0.20.[18,19] The correlation of total respiratory scores with SpO_2 was determined using Spearman tests, considering ≤ 0.25 as little or no correlation, fair if within the range 0.25–0.50, moderate to good if within the range 0.50–0.75, and good to excellent if ≥ 0.75.[20] A p value of less than 0.05 was considered statistically significant.

Results

Sixty children were enrolled (median age of 6 (4–10) months) of which 51.7% had six months or less and 21 were male (54.5%). Ten children had a history of prematurity or presented a previous diagnosis of a cardiopulmonary disease. Moreover, 50% of the children were diagnosed with a first episode of bronchiolitis. The baseline characteristics of the sample, according to the age group ($<=$ or >6 months of age), are depicted in Table A.1.

The median value of SpO_2 was 96% (93–98) upon admission and 97% (95–99) at discharge. In the emergency department, 15% of children ($n = 9$) were managed without specific therapeutic interventions while all the others were treated with bronchodilators, hypertonic saline, and/or oral steroids. Oxygen was prescribed in 3.3% of cases ($n = 2$) (Table A.1). 75% ($n = 45$) of the children were discharged from the emergency department (Table A.1).

The data collected through the WRS and KRS respiratory scores are detailed in Table A.2. The median (IQ) score of WRS was 5.5 (4–7) and 6 (5–9) upon admission, and 3 (2–5) and 5 (3–7) at discharge, for the first (physician) and second (physiotherapist) observer, respectively. The median score of KRS was 4 (3–5) and 4.5 (4–5) upon admission, and 3 (2–4) and 3 (3–5) at discharge, for the first and second observer, respectively.

There was a fair correlation between KRS/WRS and SpO_2 upon admission and discharge for the first observer and the second observer (Table A.3). The inter-rater reliability was good for KRS (ICC 0.78) and moderate for WRS (ICC 0.69), with a power of 0.756 (Table A.3). Internal consistency of KRS was graded as sufficient with a Cronbach α ranging from 0.43 to 0.78 (Table A.4). The inter-rater reliability for individual clinical signs in KRS was similar to WRS, with weighted kappa ranging from 0.21 (0.04–0.39) to 0.50 (0.33–0.68), and the respiratory rate presented the highest reliability with a kappa value of 0.50 (0.33–0.68), followed by chest recession with 0.46 (0.23–0.64), skin color with 0.46 (0.13–0.78), breath sounds with 0.36 (0.15–0.57) and general condition 0.21 (0.04–0.39) (Table A.4).

Discussion

In this study, we report a sufficient internal validity and good reliability of both scoring systems, when applied by physicians and a physiotherapist to assess the clinical severity of a child's observed bronchiolitis in the setting of a busy emergency department. Both scores performed well with each item significantly contributing to the overall score. The correlation with SpO_2 was fair in both scores and the inter-rater reliability obtained a correlation magnitude higher in the KRS than in the WRS.

The SpO_2 determined by pulse oximeter is usually used by physicians to establish bronchiolitis severity, but should be considered alongside other factors such as respiratory frequency, heart rate, age and feeding intake to get the most accurate assessment of bronchiolitis level of severity.[3,21,22] The average negative correlation between SpO_2 and both respiratory scores obtained in our study was similar to that reported by Chin and Seng.[14] The fair correlation could not be seen as a negative outcome because a large fluctuation of SpO_2 is normal during a bronchiolitis episode and it is normal to observe low levels of SpO_2 in light or moderate bronchiolitis.[22] This could be the reason for the fair correlation with both scores.

Despite the fact that the physician's level of experience varied considerably, the inter-rater agreement was found to be good. The respiratory rate was shown to be the best parameter to determine respiratory distress in both scores and for both observers, followed by breath sounds/wheezing in WRS and chest recessions in KRS. These findings were expected and other researchers have also previously reported that objective physical signs present a higher inter-rater agreement than subjective physical signs.[9,23]

General condition showed to be the least reliable parameter in both respiratory scores. This may be explained in part by the brief explanation of scores given to first observers and by the subjectivism of this parameter. In the case of KRS, observers had a footnote explaining that under 'General Condition', observers should assess the general complexion of children in addition to asking caretakers if they had noticed a food intake decrease or change in sleeping pattern. However, in the case of WRS, observers did not have this kind of guidance and could only score as zero or three upon a simple observation of children complexion at that moment. This might have led to doubt in cases with small decreases in nutrition intake or slight alteration in sleeping pattern — in most cases, these were recorded as a zero when they should have been recorded as 3.[9,10]

Our study did not aim to determine a model for predicting admission but to examine the inter-rater agreement of the scoring system when used by different health professionals with different levels of experience, not only for clinical purposes but also for research purposes. We can consider that this objective was accomplished as we reported an inter-rater reliability higher than 0.70, with KRS obtaining 0.78 and WRS 0.69.

One of the identified strengths of our study was the fact that among the participants not only children with a first episode of bronchiolitis were included, but also children with exclusion factors (e.g., cardiopulmonary disease, prematurity) allowing us a larger generalization in terms of population. Another positive aspect was the fact that the assessments between observers were all performed within 15 min of each other — this not only followed the practice in other studies[7,24] and allowed comparison, but also reduced the probability of having the change in the children's clinical condition interfering with the clinical score assignment.

Most of the previous comparative studies between two scores, or treatments efficacy studies using one specific score, were conducted in inpatients and only few studies have been conducted in an emergency department environment and outpatients.[21,25–27] This is probably due to the fact that it is easier to obtain a sample of hospitalized patients than that of outpatients, since it is unpredictable when eligible patients access the emergency department and are in conditions to be discharged home. In our study, although recognizing the challenges of recruiting patients in the emergency department, we specifically tried to evaluate the performance of respiratory scores used by different health professionals in an emergency department. In a hospital, this is after all the first point of call for patients with bronchiolitis and a very different setting from the regular ward, given the higher number of patients and medical personnel. It was thus a particularly positive result to find a good KRS inter-rater reliability and a sufficient internal consistency in this different setting.

Some of the limitations of our study were the sample size and the study design, which limited our capacity to assess other important properties of the scores, namely their construct validity in regard to decision to admit or discharge comparing with length of stay, and responsiveness. The number of physicians and the number of physiotherapists involved should be more balanced, given that in this study, the unbalanced distribution turned out to limit our ability to calculate a more accurate inter-rater reliability. The difference in number of physicians and physiotherapists also violated some Kappa calculation, leading to an overestimation of the results which should be taken as a reference only.

Finally, another limitation was the insufficient information briefed to physicians, with no previous contact with the respiratory scores — this has led to unforeseen difficulties which might explain some of the reported inconsistencies.

In a future larger study, the construct validity of KRS should be established to prove the utility of this score in an emergency department.

Conclusions

Both respiratory scores and most of the physical signs showed high agreement between observers. In fact, both scores present similar results in regard to their internal consistency. However, given that inter-rater reliability was higher in KRS than in WRS, KRS seems more consistent for use by health personnel in the assessment of children with bronchiolitis in the setting of an emergency room.

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Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this paper.

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Author Contributions

Frederico Ramos Pinto conceptualized and designed the study, analyzed the data and drafted the initial paper, and approved the final paper as submitted.

Inês Azevedo and Liane Correia-Costa conceptualized and designed the study, supervised data collection, participated in and supervised data analyses, reviewed and revised the paper, and approved the final paper as submitted.

Appendix A

Table A.1. Baseline characteristics of participants and selected outcomes according to age groups.

	≤6 Months ($n = 31$)	> 6 Months ($n = 29$)	p value
Demographics characteristics			
Gender, male, n (%)	21 (54.5)	19 (47.5)	0.004
Clinical history			
Prematurity, n (%)	3 (9.7)	2 (6.9)	> 0.001
Cardiopulmonary disease, n (%)	1 (3.2)	4 (13.8)	> 0.001
First episode of bronchiolitis, n (%)	20 (64.5)	13 (44.8)	0.577
Oxygen saturation			
At admission, median, IQR	97 (95–99)	96 (92–97)	0.088
At discharge, median, IQR	98 (95–100)	97 (95–98)	0.056
Hospital admission, n (%)	9 (29.0)	6 (20.7)	0.020

Notes: Values presented are n (%) or median (P25–P75); mo: months; Entr/Disch: entrance/discharge.

Table A.2. Total respiratory scores at admission and discharge, by observers.

		Admission	Discharge
WRS	1st Obs., median (IQR)	5.5 (4–7)	3.0 (2–5)
	2nd Obs., median (IQR)	6.0 (5–9)	5.0 (3–7)
KRS	1st Obs., median (IQR)	4.0 (3–5)	3.0 (2–4)
	2nd Obs., median (IQR)	4.5 (4–5)	3.0 (3–5)

Notes: WRS: Wang respiratory score; KRS: Kristjansson respiratory score; Obs.: observer.

Table A.3. Correlation of SpO_2 with totals of WRS and KRS and Inter-rater reliability between the two observers.

	SpO_2				
	1st Observer		2nd Observer		
	Admission	Discharge	Admission	Discharge	ICC
WRS	−0.299 ($p = 0.020$)	−0.313 ($p = 0.015$)	−0.295 ($p = 0.022$)	−0.409 ($p = 0.001$)	0.686 ($p = 0.001$; 95% CI = 0.475–0.812)
KRS	−0.397 ($p = 0.002$)	−0.349 ($p = 0.006$)	−0.324 ($p = 0.012$)	−0.427 ($p = 0.001$)	0.780 ($p = 0.001$; 95% CI = 0.633–0.868)

Notes: SpO_2: Oxygen saturation; WRS: Wang Respiratory Score; KRS: Kristjansson Respiratory Score; ICC: Intraclass Correlation Coefficient.

Table A.4. Internal consistency and inter-rater reliability for individual clinical signs in WRS and KRS.

		Cronbach α values	Weighted kappa (95% CI)
WRS	Respiratory rate	0.78	0.52 (0.35–0.69)
	Chest retraction	0.76	0.39 (0.19–0.59)
	Wheezing	0.68	0.50 (0.33–0.66)
	General condition	0.43	0.23 (0.03–0.43)
KRS	Respiratory rate	0.69	0.50 (0.33–0.68)
	Chest recession	0.65	0.46 (0.23–0.64)
	Breath sounds	0.70	0.36 (0.15–0.57)
	General condition	0.53	0.21 (0.04–0.39)
	Skin color	0.69	0.46 (0.13–0.78)

Notes: WRS: Wang Respiratory Score and KRS: Kristjansson Respiratory Score.

Table A.5. Wang respiratory score.

Score	0	1	2	3
Respiratory Rate (breaths/minute)	< 30	30–45	46–60	> 60
Wheezing	None	Terminal expiration or only with stethoscope	Entire expiration or audible on expiration without stethoscope	Inspiration and expiration without stethoscope
Retraction	None	Intercostal recession	Trachea-sternal recession	Severe with nasal flow
General Condition	Normal			Irritable/lethargic/poor feeding

Table A.6. Kristjansson respiratory score.

Score	0	1	2
Respiratory Rate (breaths/minute)	< 40	40–60	> 60
Chest Recession	None	Moderate (costodiaphragmatic)	Severe (as in 1 plus rib & jugular retraction)
Breath Sound	Vesicular	Wheeze +/− rhonchi/rale	Severe wheeze +/− rhonchi/rale
Skin Color	Normal	Pallor	Cyanosis
*General Condition	Not affected	Moderately affected	Severely affected

Notes: *(a) Not affected if activity and feeding is normal; (b) moderately affected if activity and feeding is less than normal and (c) severely affected if child looks ill and feeds poorly.

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CHAPTER 3 – STUDY 2

Ambulatory chest physiotherapy in mild-to-moderate acute bronchiolitis in children under two years of age – a randomised controlled trial

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TITLE

Ambulatory chest physiotherapy in mild-to-moderate acute bronchiolitis in children under two years of age – a randomised controlled trial

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ABSTRACT

Objectives: The aim of this study was to compare the role of a chest physiotherapy intervention to no intervention on the respiratory status of children under two years of age, with mild to moderate bronchiolitis.

Methods: Out of 80 eligible children observed in the Emergency Room, 45 children completed the study with 28 randomised to the intervention group and 17 to the control group. The intervention protocol, applied in an ambulatory setting, consisted of combined techniques of passive prolonged slow expiration, rhinopharyngeal clearance and provoked cough. The control group was assessed with no chest physiotherapy intervention. The efficacy of chest physiotherapy was assessed using the Kristjansson Respiratory Score at the admission and discharge of the visit to the Emergency Room and during clinical visits at Day 7 and Day 15.

Results: There was a significant improvement in the Kristjansson Respiratory Score in the intervention group compared to the control group at Day 15 [1.2 (1.5) vs. 0.3 (0.5) ; p=0.005, in the control and intervention groups, respectively], with Mean difference (95%CI) of -0.9 (-1.6 to -0.3).

Conclusion: Chest physiotherapy had a positive impact on the respiratory status of children with mild-to-moderate bronchiolitis.

Keywords: bronchiolitis, chest physiotherapy, outpatients

https://clinicaltrials.gov/ - NCT04260919

INTRODUCTION

Acute bronchiolitis is the most common lower respiratory tract infection in infants and children younger than 2 years of age. It occurs in a seasonal pattern with significant burden on infants, their families and the health care system [1]. Acute bronchiolitis is usually a self-limited condition, characterized by acute inflammation, oedema, and necrosis of the epithelial cells lining small airways, and increased mucus production. Clinically, it is typically characterized by a two to three days prodrome of coryza and cough, followed by signs of respiratory distress as nasal flaring, tachypnoea, and chest retractions, with rales, fine crackles or wheezing on auscultation [2, 3]. The severity of the acute episode of bronchiolitis is usually established by a physician, based on clinical findings [2, 4]. In most cases, the disease is mild to moderate and can be treated at home; however, 1–3% of the cases develop severe disease and require hospitalization [5, 6]. In up to 85% of the hospitalized cases, the disease is caused by respiratory syncytial virus (RSV) [2, 4].

The best treatment approach for children hospitalized with bronchiolitis remains controversial and there is still substantial variation regarding the practices followed by physicians. Current scientific guidelines recommend that the standard treatment of choice should be supportive, which includes supplemental oxygen when needed, appropriate fluid therapy, and overall a “minimal handling approach” [1, 7]. According to guidelines and systematic reviews published to date, chest physiotherapy (CP) is not recommended as a standard treatment for bronchiolitis [2, 4, 8, 9].

However, it is of note that most of these recommendations and reviews are based in studies which applied classical CP methods, such as clapping, percussion or vibration technics, to hospitalised patients with bronchiolitis. To date, very few studies have been conducted with the application of more modern CP techniques in hospitalized patients [10-12]. Furthermore, although the majority of bronchiolitis cases are mild to moderate, most of the studies conducted so far focused on more severe cases.

The few studies that tested modern CP techniques in acute bronchiolitis’ patients, such as prolonged slow expiration (PSE) and rhinopharyngeal retrograde clearance (RRC), presented favourable results, suggesting that the use of CP techniques in the management of bronchiolitis could be considered, if not recommended, in some cases, depending on the severity of the disease [10, 12, 13]. To the best of our knowledge, no randomized study has yet tested the efficacy of any kind of CP, neither classical nor more recent technics, in mild to moderate acute bronchiolitis cases managed as outpatients.

The main objective of the study was to analyse the role of a modern CP intervention to no intervention on the respiratory status of children under two years of age, with mild to moderate bronchiolitis.

METHODS

Patients

The inclusion criteria considered children up to two years of age admitted at the Paediatric Emergency Department (PED) with a diagnosis of acute bronchiolitis and clinical conditions that allowed the child to be discharged home after acute management in the PED.

The diagnosis of acute bronchiolitis was established by the attending physicians, based on the classical clinical signs and symptoms, including the presence of coryza, cough, fever, chest hyperinflation, increased respiratory rate (RR) or other signs of respiratory distress, wheezing or wheezing with crackles on auscultation, and changes of feeding routine [2, 4].

Exclusion criteria were: 1) Severe bronchiolitis: respiratory rate (RR) ≥ 70 or 50 bpm (in children younger than six months or older, respectively), global retractions, apnoea, nasal flaring, oxygen saturation (SpO_2) ≤88%, lethargy, dehydration, abnormal peripheral perfusion; 2) Need for admission to the inpatient department; 3) Presence of comorbidities, namely prematurity, chronic pulmonary or neuromuscular diseases, congenital heart diseases, trisomy 21 or other congenital malformations.

Settings

The study was conducted during two epidemic seasons, from December to March of 2011 and 2012, at the PED of a Northern Portugal tertiary hospital (Centro Hospitalar Universitário São João - Porto, CHUSJ).

All children fulfilling the inclusion criteria and none of the exclusion criteria were invited to participate and their parents/legal guardians were given detailed information on the study protocol provided by the responsible physiotherapist of the study.

The trial was registered at ClinicalTrials.gov (NCT04260919) and was reported according to CONSORT guidelines [14].

Randomization was conducted by permuted-blocks [15]. Allocation envelopes were stored in sequentially numbered (from 1 to 6), opaque, sealed envelopes, prepared by a person not involved in the study, and opened after the inclusion of a new case.

Observations and study intervention

All children were observed in a quiet environment, while awake and not crying, and were submitted to a standard protocol consisting of clinical demographic data collection, assessment of oxygen saturation using pulse oximetry and of the Kristjansson Respiratory Score (KRS) to quantify the severity of the respiratory status of the child [16-18]. Although Wang Respiratory Score (WRS) is a more widely used score, studies comparing it with KRS show that this has better interobserver reliability, a very important aspect to this study [17, 18]. This assessment was attributed to each child, at PED admission, at PED discharge, at Day 7 and Day 15.

Children allocated to the intervention group (IG) underwent a standard intervention CP protocol between PED admission and discharge, and after PED discharge. The protocol was performed by a single physiotherapist and consisted of a 20-minutes session taking place during working days in the first week (5 sessions), and every other day during the second week (3 sessions), with a total of 8 sessions. All sessions were carried out, as outpatients, in the Physical Medicine and Rehabilitation Department of CHUSJ. A series of exams were carried out in every session, namely the CP protocol, repeated lung auscultation and continuous monitoring of peripheral oxygen saturation levels and heart rate (Nonin Medical Inc., Model 3100, Plymouth, MN USA). If desaturation SpO_2<92% or signs of severe respiratory distress, such as global retractions, cyanosis or nasal flaring, fever, irritability or lethargy were identified by CP protocol initiation or occurred during the session, the intervention was immediately cancelled and medical evaluation was requested [19].

The CP protocol included the application of three different techniques: PSE, RRC and provoked cough (PC). PSE was achieved by applying bimanual pressure over the thoracic cage and the abdomen at the beginning of the expiratory phase down to the residual volume and maintained for two to three respiratory cycles [10, 20]. RRC was accomplished by instillation of isotonic saline solution (0.9% NaCl) through the nostrils, followed by mouth closure, forcing inspiration trough the nasals cavities and removing secretions from this area to the oropharyngeal cavity [21-23]. These manoeuvres were carried out during consecutive breathing cycles in order to promote the mobilization of secretions towards the proximal airways. This stimulated the mechanical receptors and made the children cough spontaneously [10, 20]. If no spontaneous coughing occurred, coughing was triggered by PC, accomplished by smoothly pressuring the trachea at the level of the suprasternal notch at the end of the inspiration [10, 20, 21].

Children from the control group (CG) were not submitted to any CP protocol and were assessed at the same moments of evaluation (admission/discharge of PED, day 7 and day 15). Both groups received similar recommendations on general support measures and were medicated, as needed, by the physician responsible for the child discharge from the PED. The assessment with KRS and SpO_2 in the PED was performed by the physician responsible for the initial assessment of the children. During the subsequent two weeks the CG was assessed by the physiotherapist responsible for the study and the IG was assessed by a physician of the Physical Medicine and Rehabilitation Department of CHUSJ.

Considering the nature of this study, a double-blind assessment was not possible, as both physiotherapist and parents were aware of the intervention.

Outcome Measures

The primary outcome was respiratory status, assessed by KRS on day 15. The secondary outcome was respiratory status, assessed by KRS on day 7. This is a 5-item score which includes respiratory rate, chest recessions/retractions, breath sound/wheezing, skin colour and general condition. Each clinical sign is scored from zero to two and the total score ranges from 0 -10, being the severity established as the total score increases (Table 1) [16-18].

Statistical analysis

Data was analysed using IBM SPSS Statistics version 23.0. Continuous variables are presented as mean and standard deviation. To check the homogeneity of groups, the t-test was used for independent samples on the continuous variables and Qui-square test for categorical variables. Differences between groups were evaluated using ANOVA. Statistically significant differences ($P<0.05$) were noted with an asterisk (∗).

The assumptions of ANOVA for repeated measures include normality, homogeneity of variances, homogeneity of the matrix of variances and sphericity [24]. In the present study, normality, skewness and kurtosis values were verified, in order to validate the results obtained from the F statistics [25]. The absolute values of skewness and kurtosis can be slightly higher than (-1.96; 1.96), namely (-3; 3) and (-7; 7), respectively, without any problem in the analysis of linear models, as in the case of ANOVA [24, 26].

After verifying each assumption, it was possible to apply ANOVA for repeated measures, proceeding with Bonferroni's post-hoc tests [25]. The main factors were tested by SPSS, while multiple comparisons were obtained by Syntax.

Ethics

The study was approved by the Ethics Committee of CHUSJ, and complied with both the Helsinki Declaration and the current national legislation. Verbal and written consent were obtained from caretakers on behalf of all children enrolled in the study.

RESULTS

During the study period, a total of 105 children were assessed for eligibility to participate in the present study but 15 fulfilled exclusion criteria (5 prematurity, 2 chronic pulmonary diseases, 2 chronic neuromuscular disease, 6 congenital heart disease) and 10 were admitted into hospital because of the severity of the respiratory distress. The remaining 80 cases, were randomly assigned to the IG (n=42) and to the CG (n=38). In the end, a total of 45 children completed the study (n=28, IG; n=17, CG) (Figure 1).Loss to follow-up was mainly due to non-attendance at scheduled re-evaluation sessions, 10/42 (23.8%) in IG and 20/38 (52.6%) in CG or by indication to be withdrawn from the study due to hospital admission following clinical worsening (IG, n=2; CG, n=1) or other clinical problems (gastroenteritis or vascular disease (IG, n=2). The children baseline demographics, parents' educational level and clinical characteristics are described in table 2. No differences were found between the groups baseline demographic or clinical variables.

Concerning the four assessments, there was a trend towards a significant improvement in KRS at Day 7, where the IG shows better results compared to the CG [mean difference (95% CI) = -0.6 (-1.3 to 0.01); p=0.054] which became a significant improvement by Day 15 [mean difference (95% CI) = -0.9 (-1.6 to -0.3); p=0.005] (Table 3).

When each assessment was compared with the following assessments, the IG had a significant improvement in the KRS score over time indicating a resolution of respiratory severity (Table 4). The CG did not show a significant improvement in KRS score when comparing discharge to the following assessments (Table 4).

Table 5 indicates the individual score items for the KRS at admission and Day 15. While there was no significant difference in any individual parameter between groups at admission, there was significant improvements at Day 15 in the IG compared to the CG in respiratory frequency and chest retractions.

An important point to mention is that there were zero cases in the intervention group that experienced clinically relevant side effects.

DISCUSSION

To the best of our knowledge, this is the first study evaluating the effects of modern CP techniques in mild to moderate bronchiolitis in an outpatient setting. In this study, aiming to analyse the impact of an ambulatory modern CP intervention based on PSE associated with RRC and PC in the recovery of mild to moderate acute bronchiolitis, in children under the age of 2, we found that the respiratory status, assessed by a respiratory score, KRS, on day 15, significantly improved in children submitted to the tested intervention, when compared to the CG.

At the second assessment, at emergency room discharge, after only one intervention in the PED, the IG showed already a trend towards a better clinical status, when compared to the CG. At the end of the intervention, the IG showed a total normalization of the respiratory status, while in the CG, a small percentage of cases presented abnormal breath sounds and signs of respiratory effort, as chest retractions. Wheezing and chest retractions indicate an increase of ventilation effort, that in acute bronchiolitis may be related to inflammation, oedema and hyperproduction of mucus [27, 28] [20]. Our results suggest that CP with PSE, RRC and PC was effective in removing secretions from the airway, decreasing bronchial obstruction and improving the respiratory status of children with mild to moderate bronchiolitis.

The reason for selecting these techniques was based in the pathophysiology of bronchiolitis in new-borns and infants who have a very different anatomy and physiology in relation to older children or adults [10, 20]. In the four studies included in a recently published Cochrane review on CP in bronchiolitis, the use of PSE was reported to be associated with a reduction of the wheezing, respiratory work and discomfort of inpatients with bronchiolitis [8]. Also, regarding RRC, there is some evidence of its effect in clearing the upper respiratory tract, and very encouraging results given that it is a non-pharmacological form of intervention without clinically relevant side effects [23, 28].

The choice of an adequate CP technique is very important in regard to the safety and efficacy of intervention in bronchiolitis. Most guidelines worldwide discourage the use of classical CP (clapping, percussion or vibration technics) or acceleration of expiration flow in hospitalized children with bronchiolitis, as there is no evidence regarding its beneficial effect on reducing the length of hospital stay or on improving health status. Moreover, some of techniques were associated with several adverse side effects, such as atelectasis, vomiting and discomfort [29-31].

Until today, only a few studies have focused on the use of more recent CP techniques in patients with bronchiolitis admitted to the hospital, leaving us with insufficient data to assess the efficacy of such techniques in improving clinical signs of upper and lower respiratory airways obstruction [11, 12, 20]. Two studies, from 2011 and 2012, show a sustained reduction in the score used, over several days, suggesting that there is an accumulative effect of the CP with the techniques of PSE and RRC [10, 11]. More recently, in 2020 a study compared the PSE and PC with high-frequency chest wall compression in out-patients with bronchiolitis [32]. This mechanical device had the same positive results as the manual techniques. Both methods were able to reduce significantly the score and increase the airways clearance[32]. Another study, carried out in Spain using the same techniques, obtained a reduction in hours of oxygen therapy during the period of hospitalization [10-12]. In our study, the score was totally reduced after two weeks of treatment.

One of the major strengths of our study was the use of some of the most recent techniques of CP in children with mild to moderate bronchiolitis in an ambulatory setting, a situation in which CP might result in a faster recovery of the respiratory status. As stated, few studies have focused on the use of PSE and RRC in acute bronchiolitis and the present study was the first to be conducted in a PED and continued in the ambulatory setting [8]. The finding that CP is a relevant option in the management of mild and moderate cases of bronchiolitis in an outpatient setting is of utmost importance, given that it has shown to help avoid long recovery periods affecting both children and their families [28, 33]. Despite limited in scope, these findings confirm recent interest in these techniques, and surely warrant further studies and the collection of more data in support of a more robust understanding of the potential advantages and safety of these techniques.

As with any study, this study had expected limitations which we would like to address at this stage. The assessment of infants with bronchiolitis is difficult due to the clinical variability of the disease and there is a lack of evidence on the best tools to assess severity [2, 28, 34]. Both physiotherapy techniques used in this study are highly specialized and need a well-trained physiotherapist to perform them. In our study, all the techniques were applied by the same physiotherapist, so results cannot not be generalized to all practitioners. Also, there was a high rate of dropout in both arms of the study. Dropout in longitudinal randomised controlled trials is common and a potential source of bias [35]. In both groups, treatment and assessment sessions non-attendance was the main reason for drop-out, especially in the CG. In this group, this might be due to the fact that the parents/caregivers did not see any advantage in coming to the hospital only for regular clinical assessment. A sham intervention could have decreased the dropout rate in the CG, but ethical and psychological questions can be raised, and administering fake procedures is uncomfortable to professionals trained to perform interventions that they believe are useful for patients [36]. Although lower than in the CG, the IG also showed a high rate of dropout. This leads us to question the number of sessions included in the present study which may be too high and cumbersome. Future studies should take this into consideration and consider a lower number of sessions to address this issue.

In conclusion, our study showed that in an ambulatory setting, a CP intervention, based on passive prolonged slow expiration associated with rhinopharyngeal clearance and provoked cough, had a positive and significant impact on respiratory status of children under 2 years old with mild to moderate bronchiolitis.

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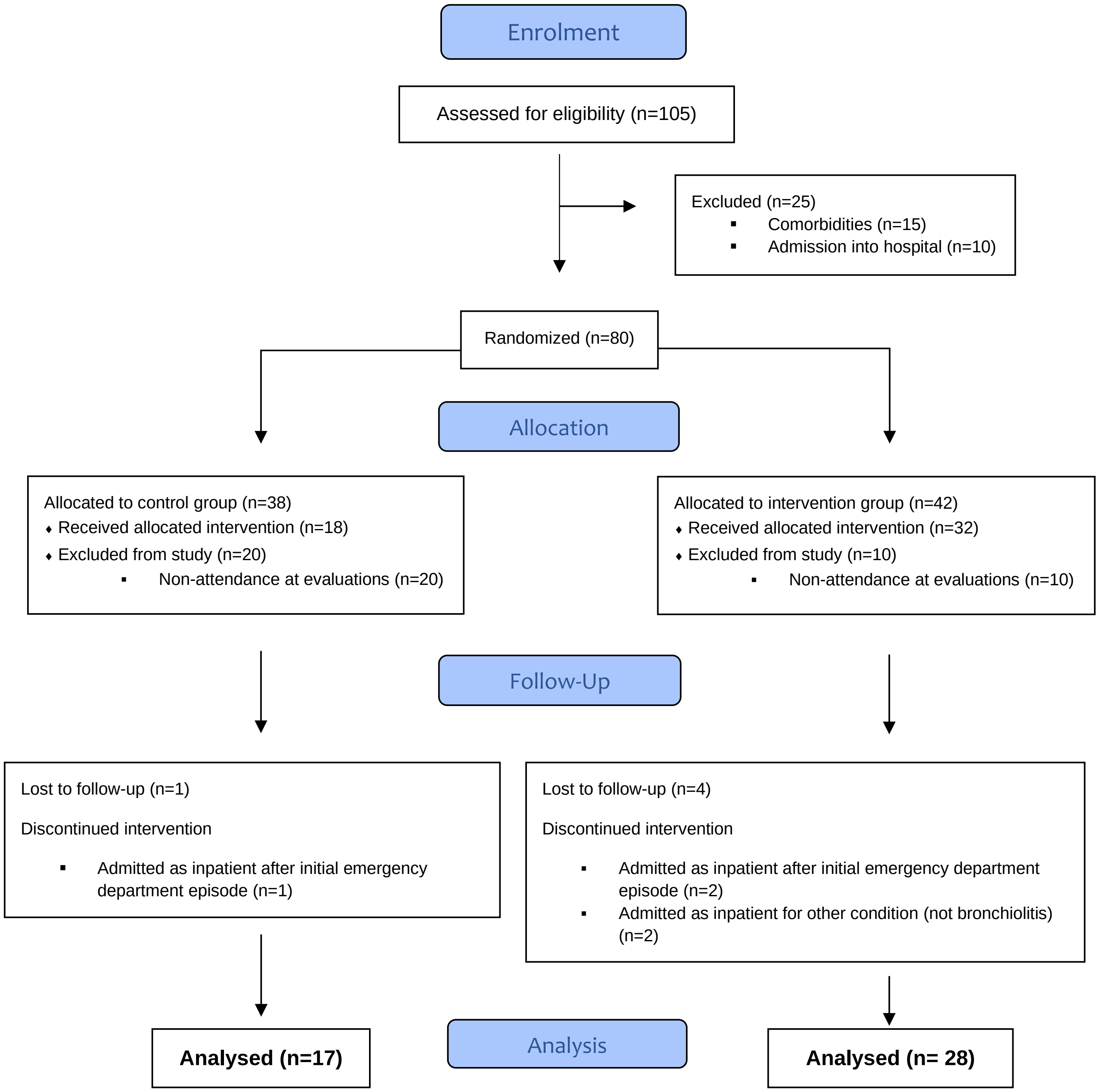
A.1

Figure 1 - Screening, Random Assignment, and Follow-up of intervention and control group.



A.2

Table 1: Kristjansson Respiratory Score

Score	0	1	2
Respiratory Rate (breaths/minute)	<40	40-60	>60
Chest Recession	None	Moderate (costal diaphragmatic)	Severe (as in 1 plus rib & jugular retraction)
Breath Sound	Vesicular	Wheeze +/- rhonchi/rale	Severe wheeze +/- rhonchi/rale
Skin Colour	Normal	Pallor	Cyanosis
*General Condition	Not affected	Moderately affected	Severely affected

* a) Not affected if activity and feeding is normal; b) moderately affected if activity and feeding is less than normal; c) severely affected if child looks ill and feeds poorly.

A.3

Table 2: Baseline demographic and clinical characteristics of the patients.

	Control Group (n=17)	Intervention Group (n=28)	p value
Demographics characteristics			
Male gender	14 (82.4)	20 (7.,4)	0.408
Age (months)	11.5 (6.737)	9.3 (5.463)	0.228
Educational level			
Father	9.00 (3.204)	9.15 (4.504)	0.909
Mother	10.35 (3.101)	10.54 (4.238)	0.878
Clinical characteristics			
First episode of bronchiolitis (yes)	11 (64.7)	14 (50)	0.372
Respiratory rate (>40 cpm)	13 (76.5)	19 (67.9)	0.737
Peripheral oxygen saturation (%)			
At admission	95.5 (1.505)	96 (2.085)	0.254
At discharge	96.7 (2.144)	97.7 (1.517)	0.082
Medication in emergency department *			
Salbutamol	16 (94.1)	26 (92.8)	
Hypertonic solution	1 (5.9)	2 (7.2)	
Ipratropium bromide	7 (41.1)	19 (67.9)	
Betamethasone	5 (29.4)	4 (14.3)	
Ibuprofen	1 (5.9)	0 (0)	
Antibiotic	0 (0)	1 (3.6)	
No medication	0 (0)	1 (3.6)	

The values presented are mean (SD) or n (%).

* Some children received more than one medication.

A.4

Table 3: Comparison of groups at each assessment with the Kristjansson Respiratory Score (KRS) (n=45).

	Assessment	**Intervention** Group Mean (SD)	**Control Group** Mean (SD)	**Mean Difference (95%CI)**	**p value**
KRS	Admission	3.4 (1.3)	3.3 (1.3)	0.1 (-0.7 to 0.9)	0.805
	Discharge	1.9 (0.9)	1.4 (1.1)	0.6 (0.0 to 1.2)	0.058
	Day 7	1.0 (0.8)	1.6 (1.3)	-0.6 (-1.3 to 0.01)	0.054*
	Day 15	0.3 (0.5)	1.2 (1.5)	-0.9 (-1.6 to -0.3)	0.005*

***** Statistically significant (p<0.05)

A.5

Table 4: Comparison between assessment in both groups (n=45).

GROUPS	Assessment (A)	Assessment (B)	Mean Difference (A-B) (95%CI)	p value
Control Group (n=17)	Admission	Discharge	1.9 (1.1 to 2.8)	<0.001*
		Day 7	1.7 (0.7 to 2.7)	<0.001*
		Day 15	2.1 (1.1 to 3.1)	<0.001*
	Discharge	Day 7	-0.2 (-1.2 to 0.8)	1.000
		Day 15	0.2 (-0.6 to 1.0)	1.000
	Day 7	Day 15	0.4 (-0.5 to 1.3)	1.000
Intervention Group (n=28)	Admission	Discharge	1.5 (0.8 to 2.1)	<0.001*
		Day 7	2.4 (1.6 to 3.2)	<0.001*
		Day 15	3.1 (2.4 to 3.9)	<0.001*
	Discharge	Day 7	1.0 (0.2 to 1.7)	0.008*
		Day 15	1.7 (1.1 to 2.3)	<0.001*
	Day 7	Day 15	0.7 (0.0 to 1.4)	0.053

***** Statistically significant (p<0.05)

nb: In this table, a positive improvement in the mean difference indicates an improvement in the KRS.

A.6

Table 5: Respiratory severity assessment of each clinical parameter of KRS, at hospital admission and after 15 days of follow-up.

		Admission (%)			Day 15n (%)		
		Control group (n=17)	Intervention group (n=28)	p value	Control group (n=17)	Intervention group (n=28)	p value
Respiratory frequency	<40	4 (23.5)	9 (32.1)	0.515	9 (52.9)	24 (85.7)	0.016 *
	40-60	10 (58.8)	17 (60.7)		8 (47.1)	4 (14.3)	
	>60	3 (17.6)	2 (7.1)		0 (0)	0 (0)	
Chest retractions	None	3 (17.6)	1 (3.6)	0.091	13 (76.5)	28 (100)	0.027 *
	Moderate	14 (82.4)	23 (82.1)		3 (17.6)	0 (0)	
	Severe	0 (0)	4 (14.3)		1 (5.9)	0 (0)	
Breath sounds	Vesicular	0 (0)	1 (3.6)	0.428	13 (76.5)	26 (92.9)	0.220
	Wheeze and rales	15 (88.2)	26 (92.9)		3 (17.6)	2 (7.1)	
	Severe wheeze ± pronounced rales	2 (11.8)	1 (3.6)		1 (5.9)	0 (0)	
General condition	Not affected	11 (64.7)	17 (60.7)	0.728	15 (88.2)	27 (96.4)	0.285
	Moderately affected	6 (35.3)	10 (35.7)		2 (11.8)	1 (3.6)	
	Severely affected	0 (0)	1 (3.6)		0 (0)	0 (0)	
Dermal coloration	Normal	16 (94.1)	25 (89.3)	0.581	17 (100)	28 (100)	a)
	Pallor	1 (5.9)	3 (10.7)		0 (0)	0 (0)	
	Cyanosis	0 (0)	0 (0)		0 (0)	0 (0)	

a)No statistics are computed because Dermal coloration at the 15th day is a constant;

***** Statistically significant ($p<0.05$)

CHAPTER 4 – GENERAL DISCUSSION

Chest physiotherapy is widely used in the treatment of children with bronchiolitis, although international guidelines do not recommend its use. This thesis sought to answer a question, which has been raised by the medical community and physiotherapists: “What is the real contribution of chest physiotherapy in children with mild to moderate bronchiolitis, who do not need hospitalization?”.

Bronchiolitis is one of the main reasons for admission to paediatric emergencies, especially in the autumn and winter periods, in temperate regions (Bryan et al., 2017). It represents a huge burden for the National Health Service, due to the large number of admissions to the emergency room and the need for hospital admission in 2% to 3% of cases, a percentage that tends to increase in recent years (Mendes-da-Silva et al., 2019). Although the majority of affected children have a self-limited condition and can be managed as outpatients, readmissions to the emergency room for reassessment are frequent (Principi et al., 2016). Some readmissions are due to clinical deterioration, but others are due to the fact that caregivers do not perceive significant improvements in the child's clinical condition, as resolution of symptoms and signs of respiratory distress and feeding difficulties may last more than 7 days and cough may persist for weeks.

Despite guidelines recommendations, in some European countries, such as France and Belgium, the prescription of chest physiotherapy for children with bronchiolitis, is frequent, both in the outpatient setting and during hospitalization (Postiaux et al., 2018; Rochat et al., 2012; Sterling et al., 2015). Our study sought to fill the lack of data to prove the effectiveness of chest physiotherapy in the ambulatory setting.

To date, all randomized studies on the application of chest physiotherapy in children with acute bronchiolitis, failed to show a reduction in the length of hospital stay or on the need of supplemental O_2, and thus guidelines do not recommend its use in the management of bronchiolitis (Gajdos et al., 2010; Ralston, Lieberthal, Meissner, Alverson, Baley, Gadomski, Johnson, Light, Maraqa, Zorc, et al., 2014; Remondini et al., 2014). However, in the latest Cochrane systematic review, the authors call attention to the fact that all randomized studies have been carried out on an inpatient basis, with classic techniques and IET (Roque i Figuls et al., 2016). Both of these techniques can have adverse effects, such as gastroesophageal reflux, tachypnoea, tachycardia and, although rarely, rib fractures (Chalumeau et al., 2002; Chaneliere et al., 2006; Gajdos et al., 2010; Gorincour et al., 2004; Harding et al., 1998). It is of notice that the studies that have used PSE, RRC and PC showed an improvement in the severity scores, which reflects a decrease in the child's breathing difficulty and an improvement in his general well-being, despite that they failed to demonstrate a decrease in the length of hospital stay (Gomes et al., 2012; Postiaux et al., 2011; Rochat et al., 2012; Roque i Figuls et al., 2016).

Up to our best knowledge, to date, no study has been conducted on an outpatient basis, raising the question if chest physiotherapy is an effective treatment for bronchiolitis in this setting, as questioned by Sterling et al. (2015). In order to answer this question, we conducted a randomized controlled study (Chapter 3 - Study 2), using PSE and RRC, techniques of choice to mobilize bronchial and nasal secretions, respectively (Gomes et al., 2012; Postiaux et al., 2014; Postiaux et al., 2011; Postiaux et al., 2018).

In order to be able to compare the effects of chest physiotherapy, in the intervention group (IG) versus the control group (CG) in Study 2, it was important to choose a scale with good inter-rater reliability, that could allow an accurate assessment of the severity level in each case. From the mid-1960s to 2013, several scales of respiratory severity were developed to assess the level of severity and progression of bronchiolitis, as well as the effectiveness of therapeutic interventions. Examples of such scores are the Tal Score (Tal et al., 1983), the Modified Tal Score (MTS) (McCallum et al., 2013), the Respiratory Distress Assessment Instrument (RDAI) (Lowell et al., 1987), the Bronchiolitis Risk of Admission Score (BRAS) (Marlais et al., 2011), the Wang Respiratory Score (WRS) (Wang et al., 1992) and the Kristjansson Respiratory Score (KRS) (Kristjansson et al., 1993) but many of these scores have not been formally validated or have been only partially validated.

After reviewing the psychometric properties of bronchiolitis assessment tools, two scores were selected that obeyed to two predefined criteria (simple to apply and with good inter-rater reliability) the WRS and KRS. An analysis of Chin & Seng's study shows that both scores have a validity and inter-rater reliability above average. Nevertheless, some studies suggested that KRS might have a higher validity and inter-rater reliability than WRS (Chin & Seng, 2004).

In Study 1 of this thesis, we compared these two scores. Similarly to the results reported by Chin *et al* (Chin & Seng, 2004), we obtained an ICC of 0.78 for KRS and of 0.69 for WRS. According to Koo & Li, these values allow us to consider KRS as score with good reliability, while WRS with moderate reliability (Koo & Li, 2016). As the KRS obtained the best inter-rater reliability in our study, we selected this score to be used in the evaluation of patients to test the impact of the physiotherapy intervention performed in Study 2 of this thesis.

The Study 2 sought to investigate if the effect of chest physiotherapy, using the techniques of PSE, RRC and PC, is effective in bronchial clearance and elimination of accumulated secretions in the airways of children with bronchiolitis. The results obtained allowed us to consider that the intervention used in this randomized controlled study (Chapter 3 - Study 2) was effective in the objective of clearing the upper and lower airways, since better values were obtained in the KRS score assessment in the IG than in the CG, throughout the protocol time.

Along the intervention time, there is a trend towards better scores in the IG compared to the CG, especially at the end of the treatment, on Day 15 with mean difference (95%CI) of -0.9 (-1.6 to -0.3). (Chapter 3 - Study 2, Table 3). Both groups presented statistically significant differences in the total KRS score, from the first moment of evaluation to the other 3 moments, but from the second moment onwards there were no differences in the CG, while the IG presents significant differences (Chapter 3 - Study 2, Table 4). The comparison of the groups shows that the IG obtained a better score than the CG.

These results may be explained by the effects of the techniques used. With the use of PSE, the air travels slowly in the bronchial lumen, especially in the more distal bronchi, avoiding the collapse of these pathways. The rheological properties of the mucus change, having the characteristics of a gel, with a viscosity that allows it to penetrate the ciliary mat and an elasticity (ability to deform) that allows it to move over the tips of the cilia (Cohen, 2006; Sleigh et al., 1988; Smith et al., 2008). When these characteristics change, due to the inflammatory process caused by viruses, the mucus becomes more viscous, causing the cilia to penetrate more into the surface layer, preventing them from moving with the ideal frequency, leading to stagnation and creation of bronchial obstruction (Houtmeyers et al., 1999). Acting on the rheological properties of the secretions, the bronchial conductance is normalized, allowing the child to regulate the respiratory rate and lung volumes, starting to have normal ventilation / perfusion, with no signs of desaturation.

If bronchial clearance and normalization of mucociliar cleaning mechanisms are important for improving ventilation / perfusion, in the case of upper airway clearance, RRC is essential for this clearance and for the child's general well-being (Alexandrino et al., 2017). By clearing the nasal passages, we improve the passage of air, allowing the child to breathe through the nose. This is essential in a small child, especially up to 6 months of age, as this way he can eat (suck) normally, not having to constantly stop sucking to be able to breathe through his mouth. All of these results indicate that the CG maintained some signs of respiratory difficulty, whether it was chest retractions, wheezing or increased respiratory rate. The chest retractions and the increase in respiratory rate arise when there is a decrease in bronchial conductance, which is caused by a decrease in bronchial calibre, a consequence of the inflammatory process of bronchiolitis. This decrease in calibre is caused by the accumulation of secretions and oedema of the bronchial mucosa (Anil et al., 2010; Koumbourlis, 2019; Yusuf et al., 2019). Like Gomes et al. (2012) indicate, the increase in mucus production, caused by inflammation, leads to obstruction, perpetuating the inflammatory process, and it is legitimate to think that reducing and eliminating excess secretions this will normalizes the bronchial calibre and, consequently, conductance bronchial, leaving no signs of breathing difficulty. Although the studies were carried out on an inpatient basis, the results achieved in study 2 are corroborated by the study by Postiaux et al. (2011) and Gomes et al. (2012), who obtained a reduction in severity scores and the study by Sanchez Bayle et al. (2012) that decreased pace of supplementary O_2 support (Gomes et al., 2012; Postiaux et al., 2011; Sanchez Bayle et al., 2012). These results suggest that there was a clearing of the bronchial tree, allowing better conductance and ventilation / perfusion.

This could explain the best results obtained in the group that had underwent chest physiotherapy, compared to the CG. All chest physiotherapy techniques applied in this study 2 aimed to eliminate excess secretions from the upper and lower airways, allowing the child to normalize mucociliar cleaning mechanisms (Gomes et al., 2012; Postiaux et al., 2011). PSE and RRC are able to detach and remove secretions that are obstructing the distal airways and nasal passages, in a safe and more comfortable way for the child. One advantage of the intervention is the possibility of teaching RRC to the child's parents / caregivers, allowing the child to keep the upper airways clear throughout the day (Alexandrino et al., 2017). This allows two important aspects to be controlled: first, in bronchiolitis with longer evolution, keeping the nasal cavities unobstructed allows the child to eat (suck) better, improving levels of hydration and well-being; second, by clearing the secretions accumulated in the nasal cavities, the risk of viral migration to the lower airways is reduced, avoiding the worsening of the bronchiolitis severity and reducing the possibility of the virus being latent in body, which can be totally eradicated from body (Alexandrino et al., 2017; Rossi & Colin, 2017; Silver & Nazif, 2019; Smyth, 2007).

All the effectiveness achieved, with the previously described techniques, in the movement of secretions into the trachea, is culminated by the coughing mechanism (spontaneous or provoked), which efficiently removes secretions from the airways (Banner, 1986; Dickey, 2018). Since cough is a reflex mechanism activated by chemical, nervous and mechanical routes, the movement of secretions up to the trachea, whether they come from the nasal fossae or the bronchial tree, creates a stimulus that triggers the reflex (Banner, 1986; Dickey, 2018). When the presence of secretions in the trachea is not enough to create a stimulus strong enough for the cough to happen, it can be triggered by putting pressure on the extra thoracic portion of the trachea (Postiaux, 2004; Postiaux et al., 2011; Postiaux et al., 2018).

The combination of these three techniques allows the physiotherapist to effectively remove the accumulated secretions in the airways, improve the mucociliar cleaning mechanisms, improve ventilation / perfusion, eliminate atelectasis caused by bronchial obstruction and unblock the nasal cavities. This allows the child to breathe with little or no effort and eat normally, significantly improving their quality of life and possibly shortening the recovery time from bronchiolitis and decreasing the likelihood of emergency readmissions due to the same episode of bronchiolitis.

The innovative and unique aspect of this thesis is probably its main strength. To the best of our knowledge, it is the first and only study to be carried out on children up to 2 years of age with bronchiolitis, treated at the first moment in an emergency department and later on an outpatient basis. All studies on the effect of chest physiotherapy on bronchiolitis, with classical techniques or with the techniques used in this study, were carried out in hospitalized children. In inpatients, the majority of children with bronchiolitis have high to severe respiratory distress, as 2% to 6% of inpatients require intensive care and, sometimes, non-invasive or invasive mechanical ventilation (Green et al., 2016). Our study focused on the vast majority of bronchiolitis cases that resort to emergencies, those with mild to moderate bronchiolitis and that can be managed at home.

We should acknowledge some limitations of our study. Despite the multiple scores for bronchiolitis, the lack of adequate studies on their psychometric properties, made it difficult to choose the ideal score to be used in study 2. This limitation made it necessary to choose the KRS and the WRS as the scales with the best psychometric properties for Study 1. Despite the evaluation of the scores in Study 1, the KRS needs a complete psychometric evaluation of its parameters. This will allow us to reach better conclusions on its validity, reliability and responsiveness. The relatively small sample size and, most importantly, the impossibility of performing a double-blind study, as the physiotherapist is always aware of the type and quality of the intervention applied, are probably the most relevant limitations that should be considered. Also, due to the impossibility of having more than one physiotherapist in the study, we cannot generalize results, as the results of the intervention are dependent on the training and performance of the physiotherapist. Moreover, if we could have had more than one physiotherapist involved, we probably would also have been able to include more patients. The loss of follow-up observed in study 2 is also of concern, especially in the control group, as non-attendance to the clinic was very high, respectively 52% in the CG and 19% in the IG, a difference that we cannot ignore. The groups were comparable in severity when randomized, but for instances lower levels of education of parents/caregivers could influence the probability of missing follow-up visits. Retrospectively, a sham intervention in the CG might have allowed us to decrease this difference, but ethical and psychological questions can be raised, since administering fake procedures is known to cause discomfort in professionals that are trained to perform interventions that they believe are useful for patients (Miller & Kaptchuk, 2004). This has led to high rate of dropout in both arms of the study. Dropout in longitudinal randomised controlled trials is common and a potential source of bias (Bell et al., 2013). In this study, several reasons led to its abandonment and the reduction of the sample size. In both groups, non-attendance at treatment or assessment sessions was the main reason, especially at the CG. In this group, this might be due to the fact that the parents/caregivers did not see any advantage to go to the hospital only for the clinical assessment established.

The uniqueness and innovation of this thesis can also be considered a limitation, since the absence of other studies, with the same chest physiotherapy techniques applied in an outpatient setting, did not allow a comparison of results.

CONCLUSION

This thesis showed that, the choice of a respiratory severity score is of utmost importance in order to be precise about the level of severity. Only in this way an ideal treatment plan can be created. in an ambulatory setting, a chest physiotherapy intervention protocol, based on passive prolonged slow expiration associated with rhinopharyngeal clearance and provoked cough, had a positive and significant impact on respiratory health condition of children under 2 years old with mild and moderate bronchiolitis. Further studies on the psychometric properties of the scores should be carried out, in order to obtain a more accurate instrument to assess the bronchiolitis severity. Additionally, more studies are needed to confirm our results but hopefully our findings will contribute to promote the emergence of more research and of fruitful discussion on the interest of chest physiotherapy on bronchiolitis management.

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CHAPTER 5 - CLINICAL IMPLICATIONS AND FUTURE PERSPECTIVES

We analysed the results of our intervention through the application of KRS, as we verified that there was a good inter-rater reliability. Despite that, present severity scores are still subjective and dependent on the observer, thus in the future there is room to try to find better tools for assessing bronchiolitis severity. Also, we did not perform a double-blind study. In future studies, the use of a sham intervention in the CG, such as classic physiotherapy techniques, that may also help to decrease the dropout rate in the CG, and the assessment of a severity score by an independent observer, that is blinded to the intervention, could add robustness to our findings.

Our results suggest that modern techniques of physiotherapy might be beneficial in mild to moderate cases of bronchiolitis, managed in in the ER and outpatient settings. However, in our study only one therapist applied these techniques, thus it is important to verify if our results can be reproduced by others, before recommending physiotherapy in the management of bronchiolitis in the ER or ambulatory setting.

APPENDIX I

REGISTRATION FORM - STUDY 1

Nº |__|__|__|

Nº episódio: _______________

Nome: ____

Data de Nascimento ___ / ___ / ___ Idade: ____ Meses Sexo: M ☐ F ☐

Filiação: ____

____

Contacto Tlf.: ________________________ Código Postal: ______

Nº |__|__|__|

FICHA DE REGISTO

Médico: ___________________________________ **Data:** ___ / ___ /___

Medicação: ____

Critérios de exclusão	**Sim**	**Não**
Prematuridade		
Malformação cardíaca		
Malformação pulmonar / torácica		
Fibrose Cística		
Displasia broncopulmonar		
Bronquiectasia		
Doença neuro-muscular		

Antecedentes pessoais	**Sim**	**Não**
Alergias alimentares (_______________________________)		
Eczema / Dermatite atópica		

Já teve outros episódios de bronquiolite? Sim ☐ Não ☐ Quantos? ____

Se sim, teve internamento? Sim ☐ Não ☐ Quantos? _______

Antecedentes familiares (pais e irmãos): Nº irmãos - _____

Doenças	**PAI**			**MÃE**			**IRMÃOS**		
	Não	**Sim**	**Se sim, foi confirmado pelo médico**	**Não**	**Sim**	**Se sim, foi confirmado pelo médico**	**Não**	**Sim**	**Se sim, foi confirmado pelo médico**
Rinite / sinusite									
ASMA									
Eczema									
Alergias alimentares									

A criança costuma estar em contacto com o fumo de tabaco na casa em que habita? Sim Não

	NÃO FUMADOR	**FUMADOR**
PAI		
MÃE		
Outros residentes		

Frequenta infantário / familiares / ama? Sim ☐ Não ☐

O seu filho(a) contacta com outras crianças? Sim ☐ Não ☐

Escolaridade (pai): ___ anos Escolaridade (mãe): ___ anos

Médico Nº |__|__|__|

S_pO_2	À entrada: ______	Na alta: ______	**Encaminhamento**	Alta		Internamento	

SCORE DE WANG

	0	1	2	3	PONTUAÇÃO	
					À entrada	Na alta
Frequência respiratória	< 30	31-45	46-60	> 60		
Tiragem	Ausente	Apenas intercostal	Traqueo-esternal	Muito acentuada com adejo nasal		
Pieira Sibilos/sibilâncias	Ausente	Presente no final da expiração (teloexpiratórios) ou apenas audível com o estetoscópio	Presente durante toda a expiração ou audível na expiração sem o estetoscópio	Audível na inspiração e expiração sem o estetoscópio		
Condição geral	Normal			Irritabilidade, letargia, falta de apetite		
				Total		

SCORE DE KRISTJANSSON

	0	1	2	PONTUAÇÃO	
				À entrada	Na alta
Frequência respiratória	< 40	40-60	> 60		
Tiragem	Ausente	Moderada (costo-diafragmática)	Severa (1 ou + espaços intercostais e adejo nasal)		
Sons respiratórios	Vesicular	Sibilância +/- crepitações	Sibilância severa +/- crepitações		
*** Estado geral**	Não afetado	Moderadamente afetado	Severamente afetado		
Coloração dérmica	Normal	Palidez	Cianose		
			Total		

***** a) Não afetado se a atividade e a alimentação for normal
b) Moderadamente afetado se a atividade e a alimentação estiverem diminuídas
c) Severamente afetado se o lactente aparentar estar doente e alimentar-se mal.

Fisioterapeuta Nº |__|__|__|

$S_p O_2$	À entrada: ______	Na alta: ______	Encaminhamento	Alta		Internamento	

SCORE DE WANG						
					PONTUAÇÃO	
	0	1	2	3	À entrada	Na alta
Frequência respiratória	< 30	31-45	46-60	> 60		
Tiragem	Ausente	Apenas intercostal	Traqueo-esternal	Muito acentuada com adejo nasal		
Pieira Sibilos/sibilâncias	Ausente	Presente no final da expiração (teloexpiratórios) ou apenas audível com o estetoscópio	Presente durante toda a expiração ou audível na expiração sem o estetoscópio	Audível na inspiração e expiração sem o estetoscópio		
Condição geral	Normal			Irritabilidade, letargia, falta de apetite		
				Total		

SCORE DE KRISTJANSSON					
				PONTUAÇÃO	
	0	1	2	À entrada	Na alta
Frequência respiratória	< 40	40-60	> 60		
Tiragem	Ausente	Moderada (costo-diafragmática)	Severa (1 ou + espaços intercostais e adejo nasal)		
Sons respiratórios	Vesicular	Sibilância +/- crepitações	Sibilância severa +/- crepitações		
*** Estado geral**	Não afetado	Moderadamente afetado	Severamente afetado		
Coloração dérmica	Normal	Palidez	Cianose		
			Total		

***** a) Não afetado se a atividade e a alimentação for normal
b) Moderadamente afetado se a atividade e a alimentação estiverem diminuídas
c) Severamente afetado se o lactente aparentar estar doente e alimentar-se mal.

APPENDIX II

REGISTRATION FORM - STUDY 2

Nº |__|__|__|

Nº episódio: ________________

Nome: ____

Data de Nascimento ___ / ___ / ___ Idade: ____ Meses Sexo: M ☐ F ☐

Filiação: ____

____

Contacto Tlf.: _________________________ Código Postal: ______

Nº |__|__|__|

FICHA DE REGISTO

Médico: ___________________________________ **Data:** ___ / ___ /___

Medicação: ____

Critérios de exclusão	**Sim**	**Não**
Prematuridade		
Malformação cardíaca		
Malformação pulmonar / torácica		
Fibrose Cística		
Displasia broncopulmonar		
Bronquiectasia		
Doença neuro-muscular		

Antecedentes pessoais	**Sim**	**Não**
Alergias alimentares (_______________________________)		
Eczema / Dermatite atópica		

Já teve outros episódios de bronquiolite? Sim ☐ Não ☐ Quantos? ____

Se sim, teve internamento? Sim ☐ Não ☐ Quantos? _______

Antecedentes familiares (pais e irmãos): Nº irmãos - _____

Doenças	**PAI**			**MÃE**			**IRMÃOS**		
	Não	**Sim**	**Se sim, foi confirmado pelo médico**	**Não**	**Sim**	**Se sim, foi confirmado pelo médico**	**Não**	**Sim**	**Se sim, foi confirmado pelo médico**
Rinite / sinusite									
ASMA									
Eczema									
Alergias alimentares									

A criança costuma estar em contacto com o fumo de tabaco na casa em que habita? Sim Não

	NÃO FUMADOR	**FUMADOR**
PAI		
MÃE		
Outros residentes		

Frequenta infantário / familiares / ama? Sim ☐ Não ☐

O seu filho(a) contacta com outras crianças? Sim ☐ Não ☐

Escolaridade (pai): ___ anos Escolaridade (mãe): ___ anos

Nº |__|__|__|

S_pO_2	À entrada: ______	Na alta: ______	Encaminhamento	Alta		Internamento	

SCORE DE KRISTJANSSON					
				PONTUAÇÃO	
	0	1	2	À entrada	Na alta
Frequência respiratória	< 40	40-60	> 60		
Tiragem	Ausente	Moderada (costo-diafragmática)	Severa (1 ou + espaços intercostais e adejo nasal)		
Sons respiratórios	Vesicular	Sibilância +/- crepitações	Sibilância severa +/- crepitações		
*** Estado geral**	Não afetado	Moderadamente afetado	Severamente afetado		
Coloração dérmica	Normal	Palidez	Cianose		
			Total		

* **a)** Não afetado se a atividade e a alimentação for normal
b) Moderadamente afetado se a atividade e a alimentação estiverem diminuídas
c) Severamente afetado se o lactente aparentar estar doente e alimentar-se mal.

APPENDIX III

INFORMED CONSENT

CONSENTIMENTO INFORMADO

O seu filho(a) tem, neste momento, uma bronquiolite aguda.

Esta doença, caracterizada por tosse, pieira e falta de ar é, muitas vezes, um episódio isolado provocado por um vírus. No entanto, alguns bebés voltam a ter episódios semelhantes nos meses seguintes, com necessidade de cuidados médicos frequentes.

Com o objetivo de avaliar a gravidade da doença e qual a importância do bebé ser tratado pela fisioterapia para melhorar o seu estado clínico, elaboramos um estudo no qual gostaríamos de incluir todos os bebés com bronquiolite aguda que são internados ou recorrem ao serviço de urgência.

Tentámos que o incómodo para as crianças e famílias fosse mínimo. No entanto, solicitamos a vossa colaboração para:

- Responder a um curto inquérito
- Seguir a criança em sessões de fisioterapia, no Serviço de Medicina Física e Reabilitação até à alta clínica ou fazer parte do grupo controlo.

A sua colaboração, que muito agradecemos, é fundamental para a realização deste estudo, que poderá ter benefícios para o seu filho e nos ajudar a compreender a importância da fisioterapia na evolução desta doença.

Para qualquer esclarecimento, contactar o investigador principal Frederico Pinto (Fisioterapeuta) através do nº 931156902 ou extensão 1046 (Serviço de Medicina Física e Reabilitação).

Fui informado(a) e concordo com a colaboração na realização do estudo “Fisioterapia respiratória nas bronquiolites agudas”

Porto __ / __ / __

O progenitor ou tutor da criança

Nome: ________________________________ Rubrica: __________________