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Effectiveness of Airway Clearance Techniques in Children Hospitalized With Acute Bronchiolitis

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Summary. Objective: To evaluate the effectiveness of two airway clearance techniques (ACT's) in children <24 months hospitalized with mild to moderate bronchiolitis. Design: One hundred and three children were randomly allocated to receive one 20-min session daily, either assisted autogenic drainage (AAD), intrapulmonary percussive ventilation (IPV), or bouncing (B) (control group), ninety-three finished the study. Outcome measures: Mean time to recovery in days was our primary outcome measure. The impact of the treatment and the daily improvement was also assessed by a validated clinical and respiratory severity score (WANG score), heart rate (HR), and oxygen saturation (SaO_2). Results: Mean time to recovery was 4.5 ± 1.9 days for the control group, 3.6 ± 1.4 days, $P < 0.05$ for the AAD group and 3.5 ± 1.3 days, $P = 0.03$ for the IPV group. Wang scores improved significantly for both physiotherapy techniques compared to the control group. Conclusion: Both ACT's reduced significantly the length of hospital stay compared to no physiotherapy. **Pediatr Pulmonol. 2017;52:225–231.** © 2016 Wiley Periodicals, Inc.

Key words: airway clearance techniques; respiratory physiotherapy; intrapulmonary percussive ventilation; autogenic drainage; bronchiolitis.

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INTRODUCTION

Acute bronchiolitis is the most common lower respiratory tract infection in infants and children younger than 2 years of age and occurs in a seasonal pattern. It is mostly a self-limiting condition associated with the respiratory syncytial virus (70–85%).[1] Usually it is a mild to moderate disease, characterized by acute inflammation, edema, increased mucus production and bronchospasm, which affect the flow and permeability of the small airways, causing hyperinflation, wheezing, and even atelectasis. However in 1–3% of the cases, severe disease is developed and hospitalization is necessary.[2]

The treatment of bronchiolitis in children is largely symptomatic and supportive. Supplemental oxygen, fluid therapy, and respiratory support remain the mainstay of treatment.[3] In 2013, a Cochrane meta-analysis concluded that hypertonic saline (HS) significantly reduced the hospital length of stay among children hospitalized with mild-to-moderate bronchiolitis and also improved clinical severity scores. HS increases the surface liquid by its osmotic action on the submucosal edema, improves mucociliary function and facilitates airway clearance.[4] However, recent studies suggest that HS has no effect on length of hospital stay.[5–7]

Chest physiotherapy aims to clear airway obstruction, thereby decreasing airway resistance, improving gas exchange, and reducing respiratory load. It is widely used in the treatment of children with chronic respiratory disease, but has been debated for a long time as a treatment in bronchiolitis. No evidence was found that chest physiotherapy has a clinical benefit in children with acute bronchiolitis.[2,8] The latest Cochrane review concluded that chest physiotherapy (chest percussion, vibrations in postural drainage positions, and forced

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Conflicts of interest: None.

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expiratory techniques) and passive expiratory techniques showed no effect on hospital stay, oximetry, and severity scores.[9] Preliminary results on the prolonged slow expiration technique, a slow passive and progressive expiration from functional residual capacity to expiratory reserve volume, showed significant effects on clinical symptoms in moderate bronchiolitis and a cumulative day-to-day improvement. Larger randomized controlled trials are necessary to confirm these findings.[10]

Autogenic drainage (AD) is a breathing routine utilizing good body knowledge and expiratory airflow throughout the whole range of breathing from residual volume to total lung capacity. The aim of AD is to move secretions progressively from peripheral to more central airways by achieving an optimal expiratory flow progressively through all generations of bronchi without causing dynamic airway collapse.[11,12] The effectiveness of AD has been demonstrated in cystic fibrosis (CF) patients[13–15] and patients with chronic obstructive pulmonary disease (COPD).[16]

Assisted autogenic drainage (AAD) is the adaptation of AD in infants and young children not yet capable of carrying out this technique actively themselves. No data on AAD in children with bronchiolitis are available.

Intrapulmonary percussive ventilation (IPV) improves airway secretion clearance in Duchenne muscular dystrophy,[17] children with atelectasis,[18] COPD exacerbation,[19,20] tracheostomized patients,[21] and patients with acute respiratory failure.[20] Encouraging results with IPV have been obtained in patients with CF.[22,23] To our knowledge there have been no trials of IPV in children with bronchiolitis.

The primary objective of this open randomized clinical trial (RCT) was to evaluate the effectiveness of AAD and IPV in reducing the time to clinical stability and discharge from hospital in children aged less than 24 months old admitted for mild to moderate acute bronchiolitis, compared to children not receiving physiotherapy.

The impact of the treatment and the daily improvement was also assessed by a validated clinical and respiratory severity score (WANG score), heart rate (HR), and oxygen saturation (SaO_2).

MATERIALS AND METHODS

Study Population

During three consecutive bronchiolitis outbreaks from December 2012 through January 2015, patients were recruited among children under the age of 2 years, hospitalized with a first episode of bronchiolitis. Bronchiolitis was diagnosed on the basis of clinical findings, including wheezing or wheezing with crackles and respiratory distress. Children were eligible within 24 hr of admission if they presented as a mild to moderate bronchiolitis with a Wang clinical severity score ≥ 3 and ≤ 8. The Wang clinical severity scoring system assigns a value between 0 and 3 to each of four variables: respiratory rate, wheezing, retractions, and general condition (Table 1). A higher Wang score indicated a worse condition.[24] Exclusion criteria were: Wang score <3 and >8, comorbidities such as cystic fibrosis, neuromuscular, or congenital heart disease; respiratory distress, necessitating immediately admission to the intensive care unit, gestational age <34 weeks, immediate treatment with corticosteroids, antibiotics, or more than three inhalations with bronchodilators at hospital intake. Patients were recruited by the participating physiotherapists or by the study physician. Informed consent was obtained by one of the parents. Children were randomized to the different treatment modalities by the attribution of a computer generated number (Randomization.com, 2011), using the method of randomly permuted blocks.[25] Each number was contained in a sealed opaque envelope opened by the physiotherapist after inclusion. Envelopes were prepared by a physiotherapist, not involved in the clinical phase of the study. All pediatric department staff and parents were blind to treatment assignment.

Study Intervention

Treatment, either intervention or control, began at least 2 hr. after the latest inhalation and feeds in order to exclude their influence on the outcome measures. Children had one 20-min treatment session daily, performed by two well-trained physiotherapists in the different modalities. If no spontaneous coughing occurred, coughing was triggered every 5 min by a gentle pressure on the suprasternal notch.

Children were randomly assigned to one of the following treatment modalities during their hospital stay:

Assisted autogenic drainage: AAD is based upon the principles of autogenic drainage and used in children and patients unable to assist in the treatment. By modulating manually the functional breathing level within the vital capacity, optimal airflow will be obtained at the targeted airway generations, where secretions have been identified. AAD is carried out in a gentle and progressive way, using the patient's breathing pattern and stabilizing the child's abdominal wall to avoid paradoxical movements. A gentle increase of manual pressure on the chest during each inspiration is performed to guide the breathing of the patient towards the desired lung volume level. By restricting manually the inspiratory level the patient is stimulated to exhale slightly more than the previous breathing cycle. During expiration, the breathing movement of the patient is followed gently. No thoracic compression or excessive force is performed, which could lead to a resisting response by the patient. Feedback plays a key-roll, feeling or hearing the secretions move while avoiding any early or abnormal airway compression or

TABLE 1— Wang Clinical Severity Scoring System

	Score			
	0	1	2	3
Respiratory rate (breaths/min)	<30	31–45	46–60	>60
Wheezing	None	Terminal expiratory or only with stethoscope	Entire expiration or audible during expiration without stethoscope	Inspiration and expiration without stethoscope
Retractions	None	Intercostal only	Tracheosternal	Severe with nasal flaring
General condition	Normal	–	–	Irritable, lethargic, poor feeding

closure.[11] This manoeuvre is carried out during an individualized number of breathing cycles waiting for the child to cough spontaneously. When a spontaneous cough occurs, the manoeuvre recommences.

Intrapulmonary percussive ventilation: Intrapulmonary percussive ventilation (IPV) delivers small bursts of high-flow gas within a frequency range of 100–300 cycles/min. IPV provides a convective front of gas to the distal airways and a more homogenous distribution of alveolar ventilation. IPV promotes alveolar recruitment, helps to "unstick" mucus in small and middle-sized airways, and propels secretions cephalad to the central airways by its asymmetrical flow pattern, whereby expiratory flow exceeds inspiratory flow.[26,27] IPV was delivered using a well fitted mask with a frequency of 300 cycles/min and a pressure between 6 and 10 mbar. Each child received four cycles of 5 min of IPV. Frequency nor pressure were altered between the different cycles.

AAD and IPV were combined with bouncing. Bouncing at low amplitude (4–6 cm), a gentle up-and-down movement on a physio ball, was used to maximize the relaxation of the child, avoiding resistance against or crying during treatment.[11]

Bouncing (*B*): Control Group.

The children were well supported in upright sitting, avoiding a slumped sitting position which may in turn predispose to GOR during treatment.[11,28]

Other Interventions

All children received three inhalations daily with 0.5 ml salbutamol dissolved in 4 ml hypertonic (3%) saline (NaCl3%), nebulized over 10 min with a Sidestream nebulizer (Respironics, Pennsylvania) at a flow of 6 L/min. The children followed the same clinical treatment pathway to ensure consistent care with minimal variability of the results. Rhinopharyngeal rinsing with normal saline was applied to all patients, if needed. Oxygen supplementation was administered if SaO_2 was ≤92%. Orogastric feeding was offered to children spontaneously ingesting less than 50% of their daily needs.

Outcome Measure

Primary Outcome

The primary outcome was time from inclusion to discharge from hospital.

Secondary Outcomes

One pediatrician and two physiotherapists evaluated the Wang score variables, SaO_2 and heart rate (Mindray iMEC8, Innomediq, Belgium) before (T0), after (T20), and 1 hr after treatment (T80). They were blinded to the applied treatment. The different variables used in the Wang score showed a high level of inter-observer agreement between physicians, nurses and respiratory therapists in a multi-center study.[29] All adverse events during treatment were reported.

Sample Size

The mean time to discharge from hospital in hospitalized children <24 months with mild to moderate bronchiolitis, receiving three inhalations daily with 0.5 ml salbutamol dissolved in 4.0 ml NaCl 3% was 6 (SD 1.2) days.[30] This study was designed to detect a difference of 1 day in time to clinical stability and discharge from hospital between the different treatment modalities with a power of 90% and type one error of 5%. The calculated sample size was 31 patients in each arm.

Statistics

Demographic and clinical characteristics were compared at baseline (Table 2). Time to discharge was compared using ANCOVA with age as covariate. One way ANOVA was used to compare the mean difference of heart rate, SaO_2, and Wang score and its consisting variables, before and after (T0–T20) and before and 1 hr after (T0–T80) treatment over the period of hospital stay and on day 1 and days 1 and 2 between the three groups. Tukey's post hoc test was used for further analysis to find out group differences. The level of significance for the tests was set at 0.05. Analyses were performed using SPSS (Version 22, Chicago, IL).

TABLE 2— Infants Demographics and Clinical Severity Data

Characteristic	Bouncing (n = 31)	AAD (n = 31)	IPV (n = 31)
Age ± SD (days)	160 ± 143	121 ± 118	135 ±132
Weight ± SD (kg)	6.4 ± 2.5	6.2 ± 2.4	6.6 ± 2.2
Sex M/F	13/18	16/15	15/16
RSV+	23 (74%)	22 (71%)	23 (74%)
Oxygen/no oxygen (n)	20/11	23/8	18/13
Days of coryzal symptoms	2.0 ± 0.8	2.1 ± 0.8	2.1 ± 0.9
Time ± SD (A–I) (hours)	12 ± 6	14 ± 5	15 ± 6
Baseline Wang score ± SD	5.3 ± 0.9	5.3 ± 1.2	5.5 ± 0.9

One way ANOVA for age, number of days of coryzal symptoms before admission, time between admission (A) and inclusion (I), and baseline Wang score showed no significant differences between the three groups.

Ethics Statement

This study was approved by the UZ Brussel ethics committee (BUN143201215440) and registered at ClinicalTrials.gov (NCT02126748). All children's parents provided written informed consent.

RESULTS

Four hundred and thirty-two children with bronchiolitis were hospitalized during the study period. A total of 103 children were eligible to participate and randomized in our RCT; 33 in the IPV group, 34 in the AAD group, and 36 in the control group. Ten patients did not complete the study (two in the IPV group, three in the AAD group, and five in the control group). Nine parents decided not to continue the study trial after the first treatment, one demanded discharge from hospital. Three hundred and twenty-nine patients were not recruited, because 24% were too sick (Wang score >8), 15% were not sick enough (Wang score <3), 56% were prescribed more than three inhalations with salbutamol before inclusion, and 5% were transferred to ICU before inclusion. The data of 93 children were analyzed (Fig. 1). Children's demographics and clinical severity data were reported in Table 2. The three groups were comparable at baseline. There was no difference in clinical severity (Wang score) at admission ($P = 0.59$). The difference between the time of day of admission to hospital and inclusion in the trial for each group ($P = 0.5$) and what day of coryzal symptoms they were admitted to hospital on ($P = 0.76$) were not statistically different. Twenty children received oxygen for at least 1 day in the control group, 23 children in the AAD group, and 18 children in the IPV group (Table 2). A child was discharged from hospital if no oxygen supplementation had been given for at least 12 hr, the Wang score was normalized with minimal or no chest recession and food intake was more than two-thirds of daily needs.

Primary Outcome Measure

Both ACT's had a significant effect on time to discharge compared to the control group. The proportion of hospitalized patients in the three groups versus hospitalization time in days has been presented in Figure 2. The mean time to discharge was 4.5 ± 1.9 days for the Bouncing (control) group, 3.6 ± 1.4 days, $P_{B\text{-}AAD} < 0.05$ for the AAD group, and 3.5 ± 1.3 days, $P_{B\text{-}IPV} = 0.03$ for the IPV group. There was no difference in time to discharge between the AAD and IPV group, $P_{AAD\text{-}IPV} = 1.00$ (Table 3). The results were not substantially altered when the children aged >12 months in the different groups (n = 9) were removed.

Secondary Outcome Measures

Overall, Wang scores improved significantly at T20 and T80 for both physiotherapy techniques compared to the control group. The improvement was significantly better at T20 in the IPV group compared to the AAD group. Looking at the subscores, wheezing improved significantly at T20 and T80 in the IPV group compared to the AAD and control group. Retractions were significant lower in both intervention groups at T20 compared to the control group. Changes in HR and SaO_2 at T20 and T80 were not significantly different in the three groups (Table 3).

No changes in "general condition" were noticed at T20 and T80 between the different groups on any day. No direct complications (respiratory deterioration with oxygen desaturation, bradycardia, vomiting) due to the treatment occurred in any patient. Complications during inclusion due to bronchiolitis severity, requiring high flow oxygen therapy, antibiotics, and/or corticosteroids occurred in four children (4.3%): two patients in the control group, one in the AAD group, and one in the IPV group.

DISCUSSION

This randomized controlled trial assessed the effectiveness of two airway clearance techniques (ACT's) in children hospitalized with mild to moderate bronchiolitis. This trial showed significant clinical benefits of both ACT's compared to sham physiotherapy. Previously no benefit has been reported from chest physiotherapy techniques using postural drainage combined with clapping or passive expiratory manoeuvres in children hospitalized for bronchiolitis.[2,9,31] The use of postural drainage with head-down tilt could exacerbate gastro-oesophageal reflux (GOR) and is contra-indicated in patients with GOR.[32]

Both ACT's used in this study rely heavily on basic airway physiology to enhance clearance. There are only two physical principles to ACT's: first, there must be airflow and second, for the patient to have airflow, the patient must be able to get air behind the secretions. High

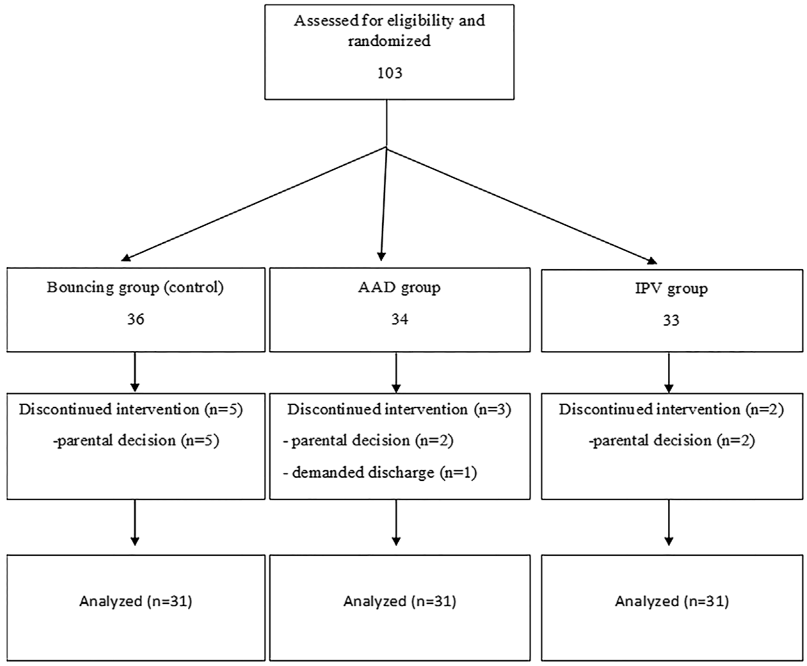

Fig. 1. Flow chart.

linear airflow velocity provides the turbulent flow, high shearing forces at the airway walls, and high kinetic energy that moves secretions cephalad.[33]

In this study, analyzing the subscores of the Wang score separately to better distinguish the impact of AAD and IPV on different respiratory and general items, wheezing improved significantly after IPV compared to AAD and control and the effect maintained after 1 hr, probably due to the positive pressure delivered by the IPV device. Cambonie et al. reported previously a sharp reduction of expiratory wheezing after 1 hr of nasal continuous positive airway pressure in children with bronchiolitis.[34] In viral bronchiolitis, characterized by inflammation, oedema, and necrosis of epithelial cells lining small airways and increased mucus production, ACT's could be efficacious in helping the clearance of airway secretions.[31] Higher sputum volumes are correlated with a higher degree of lung obstruction. In children the intercostal muscles are underdeveloped and mechanically less efficient due to the horizontal alignment of the ribs. Therefore, children depend on their diaphragm for respiration. The flatter diaphragm is mechanically less efficient and has proportionally more fast twitch fibers and fewer slow twitch (endurance) fibers and is, therefore, more vulnerable to respiratory fatigue than in the mature individual. A higher degree of obstruction leads to more respiratory distress, resulting in subcostal and intercostal retractions.[11] AAD and IPV are both effective in removing

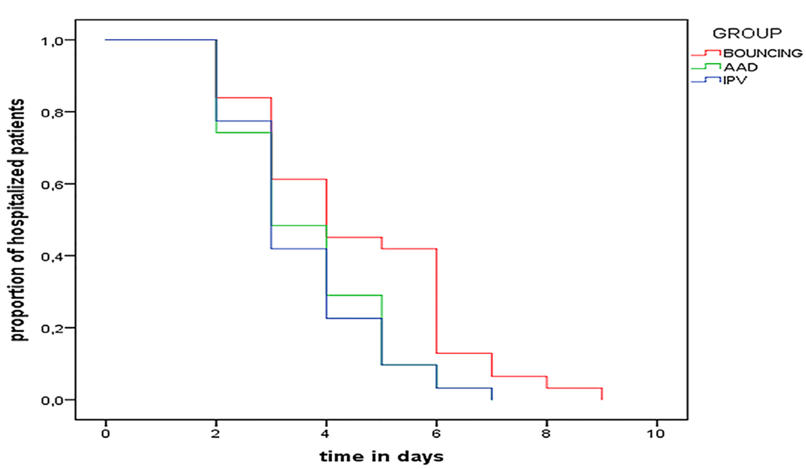

Fig. 2. Proportion of hospitalized patients versus hospitalization time.

TABLE 3— Length of Hospital Stay and Mean Differences of Wang Score, SaO_2, and HR Between the Groups Over All Hospitalization Days

	Bouncing	AAD	IPV	$P_{B\text{-}AAD}$	$P_{B\text{-}IPV}$	$P_{AAD\text{-}IPV}$
Hospital stay (days) ± SD	4.5 ± 1.9	3.6 ± 1.4	3.5 ± 1.3	0.05	0.03	1.00 NS
Wang (T0–T20) ± SD	0.2 ± 0.3	0.5 ± 0.5	0.7 ± 0.5	0.04	<0.01	0.03
Wang (T0–T80) ± SD	0.5 ± 0.4	0.8 ± 0.6	0.9 ± 0.5	0.03	<0.01	0.77 NS
HR (T0–T20) ± SD	5 ± 10	3 ± 10	4 ± 13	0.68 NS	0.86 NS	0.94 NS
HR (T0–T80) ± SD	6 ± 10	8 ± 8	7 ± 10	0.65 NS	0.93 NS	0.86 NS
SaO_2 (T0–T20) ± SD	0 ± 1	−1 ± 1	−1 ± 1	0.07 NS	0.10 NS	0.98 NS
SaO_2 (T0–T80) ± SD	−1 ± 3	0 ± 1	0 ± 1	0.91 NS	0.87 NS	0.99 NS

NS, not significant.
Hospital stay: ANCOVA for bouncing versus AAD or IPV and AAD versus IPV.
Wang score, HR, and SaO_2: Tukey's post hoc test for bouncing versus AAD or IPV and AAD versus IPV.

secretions from the respiratory tract in a short period of time. Unfortunately, there is no technique available to measure the amount of coughed up secretions in children, because they do not expectorate. Counting the number of coughs is inadequate, because dry coughs occur.

Due to the bouncing, children appeared to tolerate well both ACT's during our study and displayed no crying or distressed behavior with an increase of HR. Children even showed a significant decrease of HR in the IPV group 80 min after treatment at day 1.

In our long experience, children felt "very threatened" during respiratory physiotherapy, often leading to resistance against or crying during therapy, which decreased the efficacy or the intended effects. A significant association between crying, increased reflux episodes, and lower oxygen saturation has been recorded in children with CF.[35] Therefore, bouncing in a well-supported 90° upright position is used to maximize the relaxation of the child.

There are some limitations to this study:

A well-defined group of children hospitalized with mild to moderate bronchiolitis was selected. More research on the effect of respiratory physiotherapy is necessary in children suffering from very mild bronchiolitis managed on an outpatient basis, or severely ill children, eventually admitted to ICU.

No significant differences between the three groups in SaO_2 at T20 and T80 were observed. Differences in SaO_2 were probably wiped out by the scores of the children receiving oxygen, because SaO_2 remained 100% before, at T20 and T80 in 64% of the control group, 58% in the AAD group and 51% in the IPV group. Oxygen was administered if SaO_2 was $\leq$92%. The nursing staff recorded HR, respiratory frequency, SaO_2 and general well-being every 4 hr. Oxygen supply was decreased in a very conservative way depending on the SaO_2 and the general state of the child. It was the observers opinion that in some children too much oxygen was administered for a too long period of time, resulting in 100% SaO_2.

Although the setting in our control group was similar to the one in the study of Luo et al.,[30] we found a discrepancy in length of hospital stay (4.5 ± 1.9 days in our control group vs. 6.0 ± 1.2 days in Luo's study). A possible explanations could be Wang scores at admission in Luo's group (5.8 ± 1.2) were slightly worse than in our control group (5.3 ± 0.9).

A fourth group combining AAD and IPV would have been of interest to detect a possible strengthening effect of both techniques.

Both physiotherapy techniques used in this study are highly specialized and need a well-trained physiotherapist to perform. Equipment for IPV is unfortunately very expensive and not available in every hospital to perform these treatments.

CONCLUSION

This study showed the effectiveness of AAD and IPV, combined with bouncing, in this well-defined group of hospitalized children with mild to moderate bronchiolitis. Both ACT's reduced significantly the length of hospital stay and some respiratory symptoms of bronchial obstruction compared to no physiotherapy. It is important to recall that these observations cannot be extended to outpatients or critically ill children, whether admitted to ICU or not. Further research is necessary.

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