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ORIGINAL ARTICLE

Value of Nasal Continuous Positive Airway Pressure in the Management of Infants with Acute Bronchiolitis.

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ABSTRACT

Background: Acute bronchiolitis is one of the most common reasons for hospital admission in infancy. Treatment depends on humidified oxygen (O2), properly administered fluids, and adequate nutrition. The aim of this work is to assess the value of CPAP in the management of infants with severe bronchiolitis in the PICU.

Methods: 32 infants younger than one year old with severe bronchiolitis were recruited. Cases were divided randomly into two groups; Group A, used the standard treatment, and Group B, used nasal CPAP. Primary assessment was done for infants by recording baseline vital signs, grade of respiratory distress, and capillary blood gases. Re-evaluation was done after 12 hours and 24 hours. Evaluation of the outcome was done for the length of PICU stay, hospital stay, the need for mechanical ventilation and any complications.

Results: In the CPAP group, a significant improvement in respiratory distress was found after 24 hours. There was a significant improvement in O2 saturation after 24 hours (P<0.01). There was a significant increase in PH (P<0.01) with a significant decrease in CO2 after 24 hours (P<0.01). Improved outcomes were noticed in the CPAP group with a decrease in the duration of PICU and hospital stays (P< 0.05).

Conclusion: Nasal CPAP rapidly decreased the respiratory muscle work and improved the blood gases, which resulted in a decrease in the PICU, and hospital stay, suggesting the importance of rapid initiation of CPAP in the more severe forms of the disease.

Key words: Acute bronchiolitis; CPAP; PICU.

INTRODUCTION

Bronchiolitis is considered one of the most common causes of hospital admission among young children, especially during the first 24 months of life [1]. Although bronchiolitis is a self-limiting condition, its hospitalization rate has increased during the last two decades. This may be due to an increased incidence of risk factors such as premature births, artificial feeding, and household smoking [2]. Supportive therapy, in the form of supplemental oxygen (O2), fluid therapy, and respiratory support, remains the mainstay of treatment due to the lack of effective pharmacotherapy [3]. Several clinical studies have suggested that CPAP is beneficial in cases of acute bronchiolitis. In this disease, the critical narrowing in the peripheral airways results in severe obstruction. During the expiratory phase of respiration, dynamic collapse of the airways produces a decrease in airflow, leading to hyperinflation. This leads to a decrease in compliance and adversely affects the work required to initiate inspiration. In response to this, the respiratory rate increases. Nasal CPAP improves the work of breathing, mainly by decreasing the dynamic collapse of the airways. This airway recruitment helps to empty the lungs during expiration, thereby decreasing hyperinflation and the work of breathing [4].

METHODS

Patients and study design: In this clinical trial, we included infants less than one year who were admitted to the pediatric intensive care unit with classic features of severe acute bronchiolitis with O2 saturation less than 92% in room air by pulse oxymeter.Infants with congenital heart disease, neuromuscular disease, face dysmorphism impairing the use of nasal prongs, family history of bronchial asthma, and those who were indicated for invasive ventilation from the start were excluded

from the study.This work was agreed by the Institutional Review Board, Faculty of Medicine, Zagazig University, and informed consent was acquired from parents. The study was done according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. **Study protocol:**

-Full history was taken, including history of present illness, prematurity, past, immunization, feeding, developmental, family, and social history.

-Full clinical examination, including:

Vital signs: core body temperature, respiratory rate, blood pressure, heart rate, and O2 saturation.

-Chest examination: For signs and degree of respiratory distress (RD) by assessment of respiratory rate, chest retractions and working accessory muscles. Auscultation of both lungs for detection of any crepitation or rhonchi.

Other systems examination to exclude any congenital anomaly or underlying disease that may affect the outcome

-Laboratory investigations in the form of capillary blood gases, complete blood count, and C-reactive protein were done.

-Chest x-ray (CXR) was done for exclusion of pneumonia and other diagnoses.

Patients were randomly allocated in 2 groups. Group (A) received standard treatment in the form of adequate hydration by intravenous route and O2 by nasal prongs or face mask. Group (B) nasal CPAP was used with a pressure of 5-6 cm H2O.

Both groups were given supplemental O2 to achieve an O2 saturation level above 92%, as recorded by the pulse oxymeter. Corticosteroids, bronchodilators, and adrenaline were not used.

The follow up of cases was done over 24 hours by capillary blood gases every 12 hours, pulse oxymeter continuously during the study. Clinical data, including heart rate, respiratory rate, and chest retractions, was recorded every 12 hours. Documentation was done for any clinical deterioration, apnea, worsening hypercapnia, hypoxia, and the need for invasive ventilation.

STATISTICAL ANALYSIS

The collected data was entered and analyzed using the Statistical Package for Social Science (SPSS 20). Mean and Standard deviation (± SD) for parametric numerical data, median and Interquartile range (IQR) for non-parametric numerical data and frequency and percentage of non-numerical data.A Student's t test was used to assess the statistical significance of the difference between the two study group means. The Mann Whitney U test was used for data that was not normally distributed. A Chi-Square test was used to examine the relationship between two qualitative variables. Fisher's exact test was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of the cells. The statistical significance was set at $p < 0.05$ and was highly significant when p was below 0.01.

RESULTS

There were no significant differences between the two groups regarding demographic data (age, gender, mode of delivery, gestational age, history of NICU admission, and duration of symptoms) (Table 1).Also on admission, there were no significant differences between the two groups regarding vital data like blood pressure, temperature, heart rate, respiratory rate, or O2 saturation (Table 2). Also, there was no difference in laboratory (CBC and CRP) (Table 2), and radiological (CXR) (Table 3) before the start of management.

On follow up: In the CPAP group, a significant improvement in RD was found (Figure 1) and a significant improvement in O2 saturation after 24 hours (P<0.01) (Table 4). There was a significant increase in PH (P<0.01) with a significant decrease in CO2 after 24 hours (P<0.01) (Table 5). Improvement in outcome was noticed in the CPAP group with a decrease in the duration of PICU stay (P< 0.05) and hospital stay (P< 0.05). The single case that needed mechanical ventilation was in the traditional group (Table 6).

Table 1: Comparison between traditional and CPAP groups as regard personal and medical characteristics

		Group				Test of significance	
		Traditional		CPAP			
		Mean / N	SD / %	Mean / N	SD / %	P- Value	Significance
Age		3.44	1.99	3.94	1.78	0.46 (T)	NS
Duration of Symptoms		3.31	1.20	3.13	0.62	0.583(T)	NS
Gender	Female	8	50.0%	4	25.0%	0.144(C)	NS
	Male	8	50.0%	12	75.0%		
Prematurity	No	12	75.0%	12	75.0%	1.00(F)	NS
	Yes	4	25.0%	4	25.0%		
Delivery	CS	14	87.5%	12	75.0%	0.654(F)	NS
	NVD	2	12.5%	4	25.0%		
NICU	No	11	68.8%	9	56.3%	0.465(C)	NS

	Group				Test of significance	
	Traditional		CPAP			
	Mean / N	SD / %	Mean / N	SD / %	P- Value	Significance
Yes	5	31.3%	7	43.8%		

(T) T-test of significance.
(C)Chi-square test of significance.
(F) Fisher's exact test of significance.
NS= not significant

Table 2: Comparison analysis of laboratory & vital data between traditional and CPAP groups.

	Group				T test of significance	
	Traditional		CPAP			
	Mean	SD	Mean	SD	P-value	Significance
Systolic blood pressure	83.56	5.20	83.94	6.39	0.857	NS
Diastolic blood pressure	50.94	11.66	48.94	5.94	0.547	NS
Temperature	37.34	0.52	37.35	0.45	0.971	NS
Hb	11.20	1.20	12.03	1.42	0.084	NS
Plt	429.88	171.48	332.50	135.54	0.085	NS
TLC	9.96	3.59	10.68	3.41	0.566	NS
CRP	4.59	2.35	5.38	2.34	0.35	NS

NS= not significant.

Table 3: Comparison analysis of CXR findings between traditional and CPAP groups.

		Group				Test of significance	
		Traditional		CPAP			
		Number	%	Number	%	P- value	Significance
Increased bronco-vascular markings	No	2	12.5%	0	0.0%	0.484(F)	NS
	Yes	14	87.5%	16	100.0%		
Hyperinflation	No	12	75.0%	7	43.8%	0.072(C)	NS
	Yes	4	25.0%	9	56.3%		

(F) Fisher's exact test of significance.
(C) Chi-square test of significance.
NS= not significant

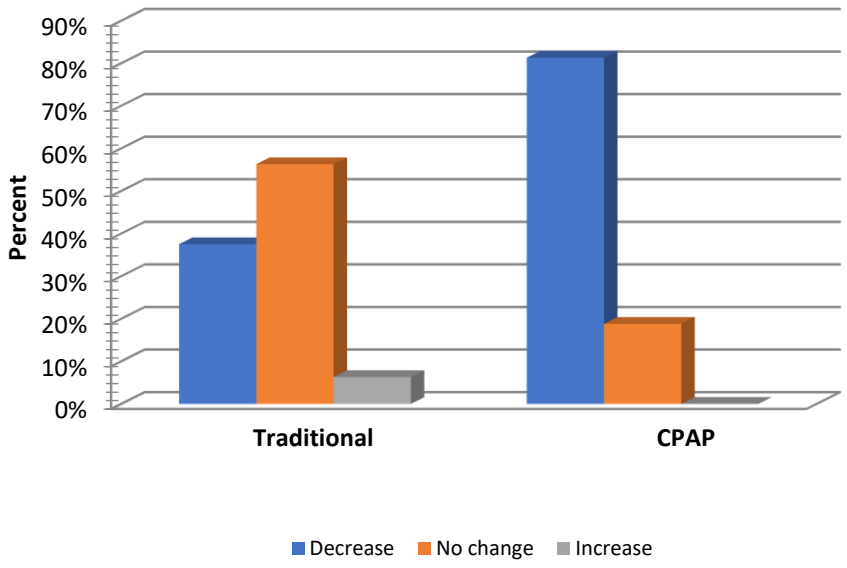

Figure 1: Comparison analysis of respiratory distress (RD)grade between traditional and CPAP groups.

Table 4: Comparison analysis of change in the vital data after starting management between traditional and CPAP groups.

	Group				Test of significance	
	Traditional		CPAP			
	Mean / Median	SD / interquartile range	Mean / Median	SD / interquartile range	P-value	Significance
HR on admission	153.00	7.72	154.75	16.77	0.708(T)	NS
HR at 12 hrs.	148.50	11.55	145.44	11.77	0.463(T)	NS
HR at 24 hrs.	147.06	12.83	142.44	13.45	0.328(T)	NS
Decrease in HR	9.0	(-4.0 - 13.0)	11.0	(3.0 - 17.0)	0.265(M)	NS
RR on admission	55.63	9.56	62.06	9.68	0.068(T)	NS
RR at 12 hrs.	55.13	9.32	53.19	9.76	0.57(T)	NS
RR at 24 hrs.	52.06	10.28	47.56	9.49	0.208(T)	NS
Decrease in RR	8.0	(-6.0 - 12.5)	15.0	(10.5 - 18.5)	0.002(M)	HS
O_2% on admission	89.44	0.89	89.13	1.36	0.448	NS
O_2% at 12 hrs.	97.06	1.18	98.06	1.34	0.033	S
O_2% at 24 hrs.	97.63	1.02	98.63	1.02	0.01	S
Increase in O_2%	8.19	1.17	9.50	1.41	0.008	HS

(M) Mann-Whitney test of significance
(T) T-Test of significance
NS=not significant.
S=significant
HS=highly significant

Table 5: Comparison analysis of CBG between traditional and CPAP groups.

	Group				Test of significance	
	Traditional		CPAP			
	Mean / Median	SD / (interquartile range)	Mean / Median	SD / (interquartile range)	P- Value	Significance
PH on admission	7.32	0.04	7.29	0.06	0.041(T)	S
PH at 12 hrs.	7.35	0.05	7.35	0.03	0.9(T)	NS
PH at 24 hrs.	7.39	0.06	7.41	0.04	0.154(T)	NS
Increase in PH	0.06	(0.03 - 0.1)	0.12	(0.1 - 0.16)	0.003(M)	HS
CO2 on admission	49.31	8.12	52.00	7.29	0.333(T)	NS
CO2 at 12 hrs.	48.94	8.85	45.88	5.14	0.241(T)	NS
CO2 at 24 hrs.	45.44	7.98	40.81	3.75	0.048(T)	S
Decrease in CO2	7.0	(0.0 - 9.0)	10.5	(7.5 - 13.5)	0.007(M)	HS
HCO_3 on admission	24.61	3.57	23.03	4.82	0.298(T)	NS

	Group				Test of significance	
	Traditional		CPAP			
	Mean / Median	SD / (interquartile range)	Mean / Median	SD / (interquartile range)	P- Value	Significance
HCO3 at 12 hrs.	25.97	2.98	24.38	2.60	0.118(T)	NS
HCO3 at 24 hrs.	26.20	3.16	24.94	1.39	0.154(T)	NS
Increase in HCO_3	1.0	(-1.0 - 4.0)	1.1	(-1.5 - 6.0)	0.955(M)	NS

(M) Mann-Whitney test of significance
(T) T-Test of significance
NS=not significant.
S=significant
HS=highly significant

Table 6: Comparison analysis of treatment and hospital admission between traditional and CPAP groups.

		Group				Test of significance	
		Traditional		CPAP			
		Mean / Median / N	SD / interquartile range / %	Mean / Median / N	SD / interquartile range / %	P-value	Significance
Duration of PICU (days)		4.12	1.21	3.31	0.87	0.075(T)	S
Hospital stay (days)		6.19	1.94	5.06	1.06	0.0498(T)	S
Need for M.V.	**No**	15	93.8%	16	100.0%	1.00(F)	NS
	Yes	1	6.3%	0	0.0%		

(T) T-test of significance.
(M) Mann-Whitney test of significance.
(F) Fisher's exact test of significance.
NS=not significant.
S=significant

DISCUSSION

Although bronchiolitis is a self-limiting condition, its hospitalization rate has increased during the last two decades. This may be due to increased incidence of risk factors such as premature births, artificial feeding, and household smoking [2].Supportive therapy, in the form of supplemental O2, fluid therapy, and respiratory support, remains the mainstay of treatment due to the lack of effective pharmacotherapy [3].CPAP action is likely to be multi-factorial. CPAP probably increases functional residual capacity, reduces airway resistance, and gas trapping in hyper inflated lungs. Ventilation of collapsed areas of the lung is improved and under-ventilated areas are recruited. In this manner, a reduction in the work of breathing and an improvement in ventilation and perfusion matching occur [5].

Two previous randomized controlled trials by Milesi et al. [6] and Cambonie et al. [7] were done to assess the use of CPAP in severe bronchiolitis. The first one recruited 19 infants less than 6 months old. They were divided like in our study into two groups, with a shorter duration of follow up (6 hours). The second study also recruited only 12 cases from a younger age group (infants less than 3 months old) for a 6-hour duration. Our study then tested the intervention in a larger group with a wider range of ages (infants less than 1 year old) and for a longer duration (24 hours).

A randomized cross-over study by Thia et al. [8] was conducted on 29 infants with moderately severe bronchiolitis that demonstrated the effectiveness of CPAP in reducing capillary PCO2 compared with O2 therapy. However, very young infants were not included in this trial and the physiological data was limited to blood gases and respiratory and heart rates, potentially explaining the absence of clinical improvement. Regarding the epidemiology, in our study we found that male infants had severe bronchiolitis more than females. This was similar to the epidemiology of the disease among the population [9]. Most of our cases were born by caesarean section. Evidence supports that elective caesareans or delivery without labor may result in impaired immunity in the newborn, leading to an increased risk of early viral lower respiratory infections [10]. Also, prematurity and a

history of NICU admission were common among our patients. This reflects the association between them, and the bronchiolitis severity as proved by Shi et al. [11]. There were no significant differences between the two groups regarding demographic data (age, gender, mode of delivery, gestational age, history of NICU admission, and duration of symptoms). This reflects that cases in both groups were matched and had the same personal characteristics. Also, on admission, there were no significant differences between the two groups regarding vital data like blood pressure, temperature, heart rate, respiratory rate, or O2 saturation. Also, there was no difference in laboratory (CBC and CRP), and radiological (CXR) findings before the start of management. This reflects that cases in both groups were clinically matched and had the same clinical characteristics, thereby avoiding any factor that may affect the response to either of the two treatment methods, either positively or negatively. Regarding the grade of RD, there was no significant difference between the two groups after 12 hours of the study. While after 24 hours, a significant improvement in the RD grade was found in the CPAP group. Overall, change in RD grade after the end of the study showed that a significant number of cases in the traditional group had no improvement in RD grade. Moreover, some cases had an increase in RD grade. This was not found in the CPAP group. Improvement of RD grade is the most important factor in determining clinical improvement, which directly affects the outcome of the disease. The results of our study were in favor of the use of nasal CPAP in such cases. This was similar to Milesi et al. [6] and Cambonie et al. [7].There was no significant change in the heart rate in both groups in our study, while it was highly significant in Figueroa and Laffaye [12] and Wen-Jue et al. [13]. Improvement in the heart rate is a good sign of improvement but not specific to the respiratory condition as it may be affected by factors like the patient's temperature and hemodynamic state.

Respiratory rate (RR) is the main determinant of the RD grade. In our study, a significant decrease in RR was found after 24 hours in the CPAP group. This was in agreement with Milesi et al. [6], Wen-Jue et al. [13], and Larrar et al. [14]. While there was no change in the respiratory rate between the groups in the study by Thia et al. [8]. The improvement of respiratory rate in the CPAP group is thought to be due to the pressure support provided by the CPAP that leads to a decrease in the dynamic collapse of the airways. This airway recruitment helps to empty the lung during expiration, thereby decreasing hyperinflation and the work of breathing.

A significant increase in O2 saturation was observed in the CPAP group starting after 12 hours, with a significant increase after 24 hours. However, no significant difference in O2 saturation was found between the two groups in the studies by Milesi et al. [6] and Wen-Jue et al. [13]. Improved oxygenation was thought to be due to the opening of the airways by the effect of the pressure support, improving the ventilation-perfusion mismatch that was found in the pathophysiology of the disease. Also, the decreased respiratory effort allowed good oxygenation to take place. This was not achieved by O2 therapy alone, like in the traditional treatment. Regarding the capillary blood gases, there was a significant decrease in CO2 after 24 hours on nasal CPAP, which denotes the improvement in ventilation in that group. This was similar to Figueroa and Laffaye [12], Thia et al. [8], Martinon-Torres et al. [15] and Wen-Jue et al. [13] results. Our study also showed a significant increase in PH with no increase in HCO3, which indicates that the improved PH is relevant to improved ventilation and decreased hypercarbia in the CPAP group in comparison with the standard treatment group. Regarding complications from CPAP, A study conducted by Smith et al. [16] concluded that PEEP in infants with bronchiolitis may increase the risk of barotrauma from air trapping. But in our study, we didn't report any clinical or radiological evidence of air leak during the course of management, either by traditional or CPAP. Similarly, Thia et al. [8], Schroeder et al. [17] and Javouhey et al. [18] didn't report such complications. In our study, no infant in the CPAP group needed a mechanical ventilator, while one infant in the standard treatment group was put on a mechanical ventilator due to respiratory failure. None of the participants in the study by Milesi et al. [6] required mechanical ventilation, whereas two patients in the control group (standard treatment first) in the study by Thia et al. [8] required mechanical ventilation. The preferred outcome for the effect of CPAP in bronchiolitis would be the avoidance of invasive ventilatory support. However, very few children with bronchiolitis require invasive ventilation, and studies using this as the primary outcome would require a multicenter trial enrolling many more children. Durations of PICU and hospital stay are important indicators for rapid clinical improvement. Our study showed a decrease in the duration of PICU stays in the CPAP group. This was due to the more rapid improvement of clinical and laboratory data than the standard treatment group. A study by Pirret et al. [19] was in agreement with our results. While no difference was found between the two groups in a study by Yanez et al. [20], this was possibly because of the

difference in severity of lung injury in both groups. A hospital stay is an important outcome also. In our study, hospital stays were noted to be shorter in the CPAP group than in the standard treatment group. In Milesi et al. [6], and Thia et al. [8] studies, there was no significant difference in the duration of hospital stay between the standard treatment and CPAP groups. This was explained by the fact that those studies were not large enough to confidently demonstrate any difference in the length of hospital stay. **Conflict of interest**: The authors of this manuscript declare no conflicts of interest, and no relationships with any companies, whose products or services may be related to the subject matter of the article.**Funding:** The authors state that this work has not received any funding.

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