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COMPARISON OF HFNC AND NCPAP IN MANAGEMENT OF BRONCHIOLITIS IN INFANTS AND YOUNG CHILDREN AT A TERTIARY CARE SETUP.

Paediatrics

Sri Ranga Modalavalasa — Junior resident in the department of Pediatrics, ASRAM medical college, Eluru , Andhra Pradesh.

Vasundhara Arigela* — Professor and HOD Pediatrics, ASRAM medical college, Eluru , Andhra Pradesh. *Corresponding Author

Venkatasriram Gutta — Senior resident in the department of Pediatrics, ASRAM medical college, Eluru , Andhra Pradesh.

ABSTRACT

Bronchiolitis is one of the common diagnoses requiring hospitalization in less than two years old children. The most commonly used treatment strategy for providing positive pressure ventilation (PPV) in these children is nasal Continuous Positive Airway Pressure (nCPAP). Recently, high flow nasal cannula (HFNC) therapy is introduced. We conducted a retrospective study on HFNC vs. nCPAP in clinically diagnosed bronchiolitis cases between July 2019 to Jan 2020, comparing the improvement in respiratory rate, heart rate, fraction of inspired oxygen (FiO2), duration of treatment, treatment failure, and length of hospital stay. A sample size of 33 children was included. The median age was 2.2 months in HFNC and 1.8 months in nCPAP group, the median baseline pCO2 was 55 mmHg in HFNC and 55.5 mmHg in the nCPAP group, and the respiratory rate per minute was 58 vs. 57 (HFNC vs. nCPAP). Respiratory rate decreased faster in nCPAP group ($p < 0.05$). FiO2 requirements decreased in the nCPAP group and increased in the HFNC group in the initial 12 hrs, after that it decreased in both the groups($p < 0.01$). Heart rate improvement was similar in both groups. Eight children (53% of HFNC group) changed systems from the HFNC to nCPAP in view of disease progression. There was no difference in treatment duration, hospital stay, or progression to BiPAP or invasive ventilation between the two groups. HFNC found to be inferior when compared to nCPAP in decreasing respiratory rate (RR) and FiO2. Further studies need to be conducted to compare the efficacy of these two bronchiolitis treatment modalities, preferably through prospective randomized trials.

KEYWORDS

bronchiolitis; children; high flow nasal cannula (HFNC); infants; nasal continuous positive airway pressure (nCPAP); non-invasive ventilation.

1. Introduction

Bronchiolitis caused by respiratory syncytial virus (RSV) or other viruses is a common cause of hospital admission in infants and young children[1]. Clinically, bronchiolitis presents with cough, wheezing, retractions, increased respiratory rate and work of breathing, fever, and feeding difficulties. In some cases, the condition worsens to respiratory failure and need ventilatory support.

In our setup, the standard treatment for infants with moderate-severe bronchiolitis and respiratory fatigue is nasal continuous positive airway pressure (nCPAP). The mechanism of nCPAP is not fully understood, but the positive pressure is thought to decrease the inspiratory resistance and this relieve muscular work and improve alveolar ventilation [2], nCPAP has been shown to remove airway occlusion and increase diaphragmatic tone [3] and also nCPAP has been shown to be better than standard care in improving outcomes and decreasing pCO2 [4,5]. Still, the evidence is scarce and two reviews, among them a Cochrane review [6,7], have concluded that more randomized trials should be done to evaluate the efficacy of nCPAP in bronchiolitis.

In the past decade, the high flow nasal cannula (HFNC) therapy was introduced as an alternative method for managing respiratory distress caused by bronchiolitis. HFNC delivers high flow, heated, humidified air, and the FiO2 can be varied between 21% to 100% [8].

HFNC, similar to nCPAP, is a high flow system and is able to generate a positive pharyngeal pressure[9]. HFNC reduces the upper airway dead space and resistance [10,11]. HFNC is considered to be a less invasive treatment than nCPAP, better tolerated by children, and easier to handle by the staff [12]. In a few studies, HFNC has been shown to be more efficient than standard care (e.g., nCPAP) [12–14]. However, more evidence is required to show the efficacy of HFNC [15,16].

In 2019, HFNC was gradually introduced as an alternative method to nCPAP at the Department of Pediatrics ASRAM medical college. Prior to that, nCPAP was the first choice for non-invasive respiratory support. We conducted a study of HFNC vs. nCPAP in the management of bronchiolitis in infants and young children who need non-invasive respiratory support(HFNC or nCPAP) , using data from July 2019 to Jan 2020.

2. Materials and Methods

2.1 Settings and Patients

The Department of Pediatrics ASRAM medical college which serves children and adolescents aged 0–18 years with PICU facility.

In this study, bronchiolitis was defined as acute respiratory viral illness in children <2 years of age, with characteristic patterns of cough, wheeze, and respiratory distress. Criteria for respiratory support were, according to our institute protocols, a clinical decision based on signs of respiratory failure: high respiratory rate, retractions, recurrent apnea, hypercapnia, and acidosis. Failure of treatment was assessed by the physician when the clinical response to the given treatment was insufficient. In cases of failure, therapy could be changed to BiPAP or mechanical ventilation, and the children were eventually transferred to PICU from HDU(high dependency unit). During HFNC/nCPAP treatment, all children were intensively observed by residents and a trained nurse with HR, RR, FiO2, and saturation monitored hourly. Blood tests including arterial blood gas values (pH, pCO2) were measured prior to treatment and controlled as needed.

INCLUSION CRITERIA - children aged 0–2 years with bronchiolitis, and need for non-invasive respiratory support(HFNC or nCPAP). The study period was from July 2019 to Jan 2020.

EXCLUSION CRITERIA - need for invasive respiratory support, monitoring in an intensive care unit at the time of admission itself, or a history of chronic respiratory disease.

From the electronic patient records gathered the information from July 2019 to Jan 2020 and identified children who were fulfilling the inclusion criteria.

For nCPAP, we used binasal prongs, connected to a humidifier (Fisher & Paykel Healthcare®, Auckland, New Zealand). According to our protocols, the initial flow was 12 L/min. For HFNC, we used Opti flow Junior (Fisher & Paykel Healthcare®, Auckland) to deliver high flow, heated, humidified air. We used 3 sizes of nasal prongs, according to the weight of child. According to the manufacturer's guidelines the initial flow was 8 to 12 L/min, corresponding to the weight of child.

Oxygen flow was delivered as needed to both systems to maintain

SpO2 above 92%. Chest X-ray and ABG were routinely conducted in patients in need of respiratory support.

2.2 Data Management

From patient case sheets, data regarding age, sex, prematurity, weight, duration of symptoms, device, blood gas analysis, duration of treatment, treatment failure, and length of hospital stay were noted.

For this study, Respiratory Rate(RR), FiO2, and HR were noted at 0, 6, 12, 18, 24 and 48 h. In case of a transfer of device, the new device was noted from the time of transfer. In case of admission to Pediatric ICU (with or without invasive respiratory support) the case was noted as failure, and withdrawn data collection from failure.

2.3 Statistical Analysis

For the group comparisons, Wilcoxon rank-sum test was used because data was generally not normally distributed. Chi-square test was used for binary outcomes. Improvement in HR, RR, and FiO2 was measured using a variance-components model with maximum likelihood estimation. A squared link of time also included to investigate nonlinear effects. Device, age, sex and time, as well as interaction between time and device were chosen as explanatory variables. The model was fitted with significant variables using simple backward elimination. Post estimation analysis was conducted using residual diagnostics. For all analyses, the significance level was taken as $p < 0.05$. All statistical analyses were performed using STATA version 15 statistical software (StataCorp, College Station, TX, USA).

2.4. Ethical Approval

All procedures performed in studies involving human participants were in accordance with the institutional and national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

3. RESULTS

Total thirty three cases were reviewed and met the inclusion criteria, of which 15 and 18 patients were treated by HFNC and nCPAP, respectively. No statistically significant differences were observed in age, weight, gestational age, or gender between the two groups (Table 1). Symptom duration was reported 1 day longer at admission for the HFNC group, which was near to significance. Both groups were similar for X-ray findings (±atelectasis), HR, RR, FiO2, and pCO2 at baseline (Table 1). The nCPAP children had a median age of 1.8 (1.2–13) months and 2.2 (1.53–14.2) months in HFNC group, although the difference is not significant ($p = 0.07$). There was no significant difference in the median baseline RR (58 (51–60) vs. 57 (49–62)) or pCO2 (55 (52–60) mmHg vs. 55.5 (42–60) mmHg) between the two groups.

Table 1. Descriptive statistics.

	HFNC	nCPAP	*p*-value
N	15	18	
Gender, girls *n* (%)	10 (66)	9 (50)	Ns
Age, months, median (IQ range)	2.2 (1.53–14.2)	1.8(1.2–13.0)	Ns
Gestational age at birth, weeks + days, median (IQ range)	39+6 (37 + 3–40+3)	39 + 2 (38 + 1–40 + 0)	Ns
Weight, kg, median (IQ range)	5.2 (4.7–9.7)	5.1 (3.9–9.6)	Ns
Symptom duration, days , median (IQ range)	5 (4–7)	4 (2–5)	0.052
Atelectasis, *n* (%)	5 (33.3)	5 (27.7)	Ns
pCO_2, mmHg, median (IQ range)	55 (52–60)	55.5 (42–60)	Ns
Respiratory Rate per minute, median (IQ range)	58 (51–60)	57 (49–62)	Ns
FiO2, % (IQ range)	30 (25–35)	30 (21–35)	Ns
Pulse, per minute	161 (151–178)	156 (150–170)	Ns

IQ: Interquartile; HFNC: High flow nasal cannula; nCPAP: Nasal continuous positive airway pressure; FiO2: Fraction of inspired oxygen. Ns: Non-significant.

No differences were observed in length of hospitalization stay, duration of treatment, and transfer to PICU (Table 2).Out of 15 Patients in the HFNC group, more than half of the children(n=8) were changed to nCPAP therapy ($p < 0.001$) after a median time of 18 hours from initiation of HFNC support. The Median time to referral to PICU was 30hr, with no significant difference between the groups. The three HFNC children who were transferred to PICU had all been changed to nCPAP prior to transfer, with a median time of 11 (5–25) h from the change of system to transfer.

Table 2. Duration of treatment, Length of hospital stay, and system failure.

	nCPAP	HFNC	*p*-value
Duration of treatment, median (hours)	93.2 (60.3–163.0)	93.8 (70–146)	Ns
Length of hospital stay, median (days)	7 (4–10)	8 (5–11)	Ns
Device failure (shift to opposite, median time 18 h), *n* (%)	0 (0%)	8 (53.3%)	<0.001
Device failure (referral to PICU, median time 30h), *n* (%)	3 (16.6%)	3 (20%)	Ns

PICU: Pediatric Intensive Care Unit, Ns: Non significant.

Using the variance-component model, we found that respiratory rate decreased over time in both groups. It was found that the respiratory rate declined faster in the nCPAP group ($0 < 0.05$), independently of age and gender (Figure 1).

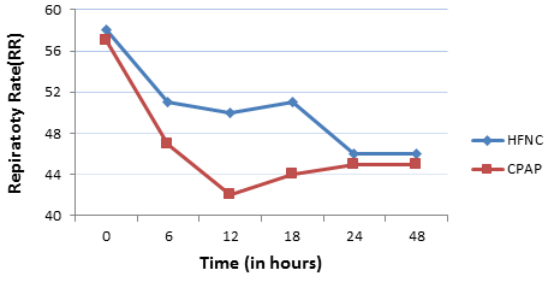

Figure 1

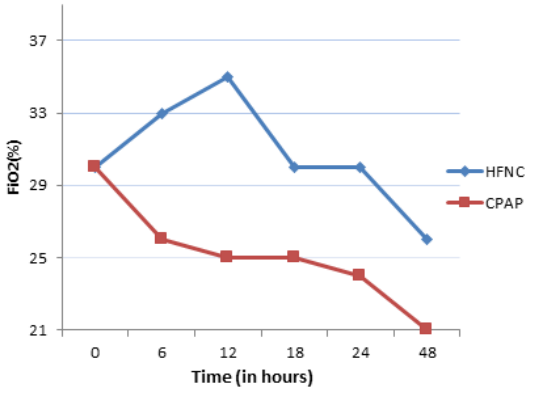

Figure 2

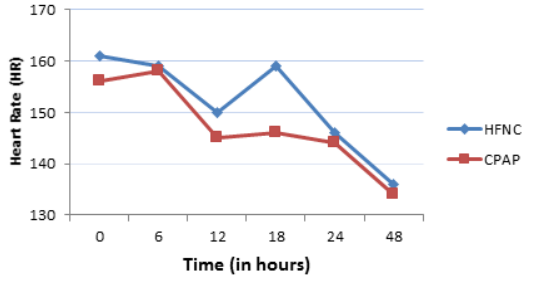

Figure 3

Figure 1. Median respiratory rate (RR), **Figure 2.** Median FiO2 and **Figure 3.** Median heart rate (HR) during 48 hrs of treatment. RR and

FiO2 decreased significantly more in the nCPAP group. HR decreased equally in both groups.

FiO2 declined over time in the nCPAP group, in the HFNC group, FiO2 increased during the initial 12 h and decreased for the rest of the treatment (Figure 2). The difference in FiO2 improvement between the groups was highly significant ($p < 0.01$).

HR came down significantly with time in both groups (Figure 3). There was no difference between the systems, and no effect of any other explanatory variable.

4. DISCUSSION

Our data suggest that HFNC was inferior to nCPAP with respect to reducing RR and the need of oxygen supply in children with bronchiolitis. Similar to our findings, Milesi et al. recently found a higher failure rate of HFNC than nCPAP in treating infants with bronchiolitis [17]. In accordance with our findings a recent study conducted by Majken et al. shows similar findings as our study in accordance to a decrease in respiratory rate and FiO2 in nCPAP group compared to HFNC group[18]. This is in opposition to Metge et al. study who found no difference with respect to RR development [19]. In this study, more than half of the patients who started treatment with HFNC were changed to nCPAP treatment, suggesting a high treatment failure with HFNC. This should be remembered that despite the diagnosis of system failure based on systematic observations of respiratory rate, respiratory work and hypercapnia, there might have been a bias in the clinical decision towards favoring nCPAP which is the well known treatment. On contrary, as shown in Figure 1 and 2, both respiratory rate and FiO2 improved after approximately 24 hrs, where many children were converted to nCPAP treatment.

The optimal pressure level of nCPAP is 7 cm H_2O. HFNC can generate a pressure of 4–5 cm H_2O[9]. However, the actual positive end expiratory pressure (PEEP) of both systems is influenced by many factors, e.g., whether the child can cooperate with the system and breathe with a closed mouth. In HFNC, the delivered pressure also depends on the nasal prongs' size and placement, whereas nCPAP, when correctly placed, is a hermetical system. We do suggest that our findings may be explained by nCPAP's better ability to keep an optimal and constant PEEP.

As mentioned earlier, in our setup, nCPAP is first line treatment for moderate to severe bronchiolitis in opposition to conservative treatment (humidified oxygen, hydration etc.). Although a few studies have shown that nCPAP is superior to the conservative treatment, evidence is scarce. Only single randomized study exists, a cross-over study comparing nCPAP with standard care[4]. Our findings of nCPAP being superior to HFNC, with respect to lowering RR and FiO2, may contribute to the evidence of nCPAP in the management of bronchiolitis.

Our study is limited by its retrospective, nonrandomized design. However, there was no significant difference in age, gender, and disease severity, measured by pCO_2, RR, pulse, and FiO2, at the inclusion time. This study's further limitations are lack of standardized measurements that could be planned in a prospective study design (e.g., a standardized clinical score and control pCO2). This study's limitations emphasize the need for prospective randomized trials comparing these two system's efficacy in treating bronchiolitis.

Though our data suggesting the better effects of nCPAP, HFNC may be a good alternative for children with less severe bronchiolitis. In this study we found no differences in treatment length, hospitalization length, or transfer to PICU, which indicates that HFNC is safe, if carefully monitored. Further studies may be able to focus on subgroups of patients benefitting from the two systems.

5. CONCLUSIONS

In our study HFNC proved to be inferior in lowering RR and FiO2 in infants with bronchiolitis. More than half of the children who started on treatment with HFNC were subsequently changed to nCPAP treatment due to suspected treatment failure. There were no differences between HFNC and nCPAP in duration of treatment, length of hospitalization, transfer to PICU or need for invasive ventilation.

Conflicts of Interest: The authors declare there are no conflicts of interests.

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