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STUDY OF EFFICACY OF HFNC IN CHILDREN WITH ACUTE RESPIRATORY DISTRESS WITH HYPOXIA IN PICU- A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Acute respiratory distress is the primary cause for admissions to paediatric critical care units. High flow nasal cannula (HFNCs) is a growingly popular method of providing respiratory assistance without intrusive measures. It has shown promise in decreasing the need for intubation. The objective of this research was to examine the effectiveness of HFNC treatment in children who have acute respiratory distress and hypoxia in a paediatric Intensive Care Unit. **Materials and Methods:** This was a prospective observational study conducted among 60 children between the age groups of 2 months and 18 years. For respiratory support, subjects were put on HFNC with an age-appropriate cannula using the Optiflow SystemR (Fisher & Paykel). The efficacy of HFNC was assessed by looking at children having successful outcome following HFNC therapy and was successfully discharged from PICU without requiring escalation of therapy or has resulted in mortality. P value < 0.05 was considered statistically significant. **Result:** The mean age of the study population in the current study was 7.25 years . The main indication for HFNC in our study was pneumonia (33.3%). The efficacy of HFNC was 80.0% in the study. The failure of HFNC in the study was 20.0%. Hospital stay was also found to be higher in those subjects who had failed HFNC (14.75 ± 2.527 days) compared to those who had successful HFNC (12.69 ± 2.485 days) (p<0.001). The mean SF ratio was found to be 215.37 ± 31.41 among the subjects who had a successful HFNC status, while it was 154.36 ± 36.58 among the subjects who had a failed HFNC status. **Conclusion:** High-Flow Nasal Cannula may be used as the first treatment for children of all age groups with different causes of acute respiratory distress in a Paediatric Intensive Care Unit.

INTRODUCTION

Respiratory diseases in children impose a substantial burden on emergency rooms worldwide. Acute respiratory distress is the primary cause for admissions to paediatric critical care units. Although invasive mechanical ventilation is an established form of supportive treatment for this illness, it is associated with higher risks of nosocomial infections, lung and airway damage, longer hospital admissions, and problems linked to sedation.

Respiratory assistance is a crucial element in the care of very unwell children. Delivery may occur invasively by an endotracheal (ET) tube or non-invasively using a face mask, nasal mask, nasal cannula, or oxygen hood. The use of invasive ventilation is linked to a higher likelihood of infection, damage to the lungs and airways, longer hospitalizations in the intensive care unit, and complications connected to sedation.

Non-invasive techniques for providing respiratory support, such as the use of nasal cannula to provide simple or high flow oxygen, as well as continuous positive airway pressure (CPAP), are alternate approaches for managing respiratory insufficiency.[1,2]

High flow nasal cannula (HFNCs) is a growingly popular method of providing respiratory assistance without intrusive measures. It has shown promise in decreasing the need for intubation.[3,4] High-flow nasal cannulas (HFNCs) provide oxygen at high concentrations while maintaining optimal humidity and temperature. This helps to enhance airway resistance and lung compliance, as well as provide a continuous positive airway pressure (CPAP) effect. Additionally, HFNCs eliminate dead space and reduce the effort required for breathing.[1,5] This therapy has been utilized in infants suffering from respiratory distress syndrome and bronchiolitis, demonstrating advantages such as reduced respiratory distress and intubation rates, improved patient comfort and ease of use in comparison to face masks or traditional cannulas, and shorter stays in paediatric intensive care units.[6,7]

Nevertheless, there is a scarcity of research investigating the usefulness of HFNC treatment in children with acute respiratory distress in a paediatric critical care unit.

The objective of this research was to examine the effectiveness of HFNC treatment in children who have acute respiratory distress and hypoxia in a paediatric Intensive Care Unit.

MATERIALS AND METHODS

Source of Data: This study was performed at the Pediatric Intensive Care Unit (PICU) at MVJ Medical College and Research Hospital over a period of 2 years, hospital based Prospective Study. Children of either sex and age between 2 months and 18 years presenting to the outpatient department and PICU with diagnosis of Acute Respiratory Distress with Hypoxia. The study was approved by the Ethical committee of MVJ Medical College and Research Hospital.

Inclusion criteria:

1. Children in the age group of 2 months to 18 years
2. Acute Respiratory Distress with Hypoxia

Exclusion Criteria

1. Patients with facial injury and facial malformation
2. Uncooperative patients
3. Critically ill children with severe respiratory distress requiring advanced respiratory support

Sample size: Total of 60 patients were considered for the study.

Sample size estimation: Sample size was estimated by using the failure rate of HFNC therapy at 15.7% and efficacy at 84.3% among children with Acute Respiratory Distress with Hypoxia from the study by Chih-Ching Chang et al., using the formula

Sample size (N) = $Z1\text{-}\alpha/2$

2 p (100-p) / d2

Where,

$Z1\text{-}\alpha/2$= Is standard normal variate (at 5% type 1error ($P<0.05$) it is 1.96.

p = Expected proportion in population based on previous study.

d = Absolute error or precision

p = 84.3

q = 100 – p = 15.7

d = 10%

Using the above values at 95% Confidence level a sample size of 51 was obtained.

Considering 10% nonresponse rate a sample size of 51 + 5.1 ≈ 60 subjects with Acute Respiratory Distress with Hypoxia was included in the study.

Type of Study: Prospective Study

Mode of selection of type of study: Hospital based prospective study

Method of data collection: Children in the age group of 2 months to 18 years presenting to the out-patient/emergency with acute respiratory distress with hypoxia were considered part of the study. Children presenting with Acute Respiratory distress was shifted to PICU were enrolled after written informed consent from the parents and then connected on HFNC. The initial Rates and FIO2 was set as per weight and age of the child.

For Respiratory support, subjects were put on HFNC with age appropriate cannula using the Optiflow SystemR (Fisher and Paykel). Routine investigations and other investigations were done as per the standard management protocol.

In the PICU the children were assessed within 1 hour for worsening of distress and the following parameters were monitored. Heart rate, Tachypnea, Increased O2 requirements, SPO2, Worsening clinical status and sensorium. Children who failed HFNC requiring escalation of airway support to NIV/ Intubation were noted. Children who improved on HFNC within 1 hour of starting HFNC were continued with HFNC Rates and FIO2 were adjusted to maintain a saturation above 95%. HFNC therapy was considered successful if there was no respiratory distress and child could be weaned off successfully from HFNC and good clinical outcome noted.

The criteria to consider weaning off from HFNC was absence of respiratory distress and SPO2 above 95%. After weaning off from HFNC if the child was not maintaining SPO2 above 95% with underlying tachypnea, but had no signs of distress such as chest retractions, tachycardia, poor respiratory breathing pattern, the child was depronged to Nasal prong Oxygen, otherwise directly depronged to Room air.

The following information was collected for all patients:

1. Demographic data and underlying clinical history
2. Clinical parameters of disease severity, including heart rate, respiratory rate, SPO2 and initial and lowest levels of SPO2/Fio2 ratio.
3. Variables after respiratory support, including initial and maximum HFNC parameters (Fio2 and flow)
4. Duration of HFNC use and outcome

Outcome of this study was to evaluate the efficacy of HFNC in PICU setting in children with Acute Respiratory distress with hypoxia and understand the risk factors for failure of HFNC in children with acute respiratory distress between the age group of 2 months to 18 years.

Efficacy of HFNC: Efficacy of HFNC was assessed by looking at children having successful outcome following HFNC therapy and successfully discharged from PICU without requiring escalation of therapy, Reduced length of stay in PICU, Child hemodynamically stable after starting on HFNC with Lower initial Fio2 and using SPO2/FIO2 Ratio where a higher ratio signified better outcome.

Failure of HFNC: Children were considered to have failed HFNC, if child had worsening of Respiratory distress, not maintaining of SPO2 above 95 % even after reaching high parameters on HFNC (>60% Fio2), low SPO2/FIO2 Ratio, clinically deterioration of the child/ hemodynamically unstable child, for which the child was escalated to other modes of ventilation such as NIV or Endotracheal Intubation.

Statistical analysis: The data was collected using Microsoft 365 Excel and analyzed using SPSS v27.0. The normality test (Shapiro-Wilk Test) was performed to analyze the data, and the results were expressed as frequency with percentage and mean with standard deviation or median with interquartile range. Association between categorical variables was assessed using Chi-square test or Fisher's exact test. Association between quantitative variables was assessed using independent t test. All the statistical analyses were carried out at a 5% level of significance, and results with the P value < 0.05 were considered statistically significant.

RESULTS & DISCUSSION

A well-received technique for respiratory support that has shown to be quite helpful in the paediatric patients suffering from acute respiratory distress accompanied by hypoxia is HFNC therapy. This therapy works by delivering heated and humidified oxygen at high flow rates, which helps to create a positive pressure environment in the airways. This positive pressure reduces resistance in the nasopharyngeal airway, leading to improved ventilation and oxygenation.

A Prospective Observational Study was conducted in a group of 60 children over a period of 2 years, ranging in age from 2 months to 18 years, who were admitted to a paediatric intensive care unit (PICU) with acute respiratory distress and hypoxia. The primary objectives of the study were to evaluate the effectiveness of HFNC therapy in managing respiratory distress in this age group and to identify any risk factors that might predict the failure of HFNC therapy.

Profile of subjects: In the present study the mean age of the study population was 7.25 years Similarly Chang et al performed their study which showed mean age of 7 years. Our study included a diverse range of paediatric patients, spanning from infants to adolescents, allowing for a comprehensive analysis of HFNC therapy across different age groups. In the present study females (51.7%) were affected more compared to males (48.3%), But in the study done by Chang et al, showed predominant male gender distribution in the subjects studied (55%).

Effectiveness of HFNC in children: The study on the effectiveness of HFNC therapy in paediatric patients with acute respiratory distress and hypoxia likely involved children with a range of underlying medical disorders. These conditions are crucial to understanding the patient population, as they can significantly impact the response to HFNC therapy and influence the overall prognosis. The main indication for HFNC in our study in children with no underlying co morbidities was pneumonia (33.3%) followed by bronchiolitis (13.3%). In our study, the subjects included children with various underlying medical conditions, such as GDD with seizure disorders (10.0%), complex febrile seizures (1.7%), Nutritional Anemia (Iron deficiency anemia) (10.0%), Anemia with CCF (3.3%), Asthma (13.4%), VSD (6.6%) and PPHN (5.0%). In the study conducted by Chang et al., the most common underlying medical conditions were, neurological disorders (27.5%), haematological disorder/ malignancy (14.7%), heart disorder (12.7%) and asthma (6.9%).

In children having underlying medical conditions, 13.3% children had respiratory distress with underlying hematological conditions (Nutritional Anemia (Iron deficiency anemia), Anemia with CCF) and 11.7% each with children who had respiratory distress with underlying cardiac condition (VSD, PPHN Thiamine responsive) and underlying neurological conditions. In the study by Chang et al., 78 children (76.5%) had underlying medical conditions. In their study the most common reasons for initiating HFNC therapy were pneumonia (40 cases, 39.2%), sepsis-related respiratory distress (17 cases, 16.7%), and bronchiolitis (16 cases, 15.7%),[8] the findings were observed to be similar to our study. According to WHO Pneumonia is the single largest infectious disease accounting for 20% of those deaths. India has a higher burden of childhood pneumonia than any other country. Infants have low immunity and immature respiratory defence which predisposes infants to pneumonia. In the study by Coletti et al., the primary indications for HFNC use included status asthmaticus (24%), status asthmaticus with pneumonia (17%), and bronchiolitis (16%) In our study second leading cause for indication of HFNC after Pneumonia was Bronchiolitis. similar to study done by Kelly et al., and Baudin et al., primary indication for HFNC was Acute Bronchiolitis.[11] Considering disease burden in our population, pneumonia cases were more in our studies.

HFNC therapy is most commonly utilised for infants with acute viral bronchiolitis. However, recent research indicates that HFNC therapy can also be effectively and safely applied to patients across a broader age range and with various causes of respiratory distress.

Vital parameters and investigations: The mean heart rate recorded before the start of HFNC in the study was 120.52 +13.85 bpm. While in the study conducted by Asseri et al., the mean heart rate was 139.7 ± 25.8 bpm.[13] This elevated heart rate may reflect the stress of acute respiratory distress. Before the start of HFNC the respiratory rate was 37.88 ± 7.78 breaths per minute. Similar study conducted by Asseri et al., the mean respiratory rate was 51.2 ± 11.8 breaths per minute. This increased respiratory rate is consistent with the participants' respiratory distress.[13]

Investigations done at the start of HFNC showed the mean Hb in the study population was 11.702 ± 1.49 g/dl, the mean WBC total count was 10120.00 ± 4866.93, and mean CRP was 43.42 ± 38.07 mg/L. Currently no data is available linking Hematological parameters to failure of HFNC.

Mean HFNC parameters: In our study the mean FiO2 required was 50.67 ± 6.701%. In the study conducted by Baudin et al., the median FiO2 required was 40.0 with interquartile range of 30.0 to 60.0%. In the Chang et al., study the mean FiO2 required was 46.93 ± 18.82 %. These results are almost identical to those in our study. The variations can be attributed to the difference in the success rate of HFNC in these studies.

The mean FiO2 administered was 54.83 ± 7.756% in those subjects who had HFNC failure and 49.63 ± 6.062 % among those subjects with successful HFNC status. This difference was found to be statistically significant. In the study conducted by Chang et al. the mean FiO2 in those who had successful HFNC was 43.27 ± 15.09 % and among those who had failure in HFNC was 68.64 ± 24.20 %.[8] Thus, a lower FiO2 is required in cases of a successful HFNC, and increased FiO2 is required before escalating to other therapies in case of failure of HFNC.

Success of HFNC: In our study the success rate of HFNC was 80.0%, which is 48 out of 60 children in our study population. In the study conducted by Chang et al,[8] the outcome of success rate of HFNC was 84.3%. In a study conducted by Kelly et al., 92% of children had success after starting HFNC early in children who presented with respiratory distress.

In conclusion, both these studies have results of success of HFNC similar to our study Various studies have been conducted which concludes that starting HFNC early is a safe and effective device to use in children presenting with respiratory distress, In addition to providing positive pressure support to the nasopharynx, HFNC provides PEEP to the lower airways, preventing alveolar collapse. which would reduce the need for invasive ventilation. Our study has shown a success rate of 80% which is similar to the other studies conducted on efficacy on HFNC.

Failure of HFNC: In our study failure of HFNC occurred among 12 (20.0%) out of the 60 subjects studied.

These children had to be escalated to other non-invasive ventilation techniques (13.3%) and endotracheal intubation (6.7%). This indicates that one-fifth of the study population required more intensive respiratory support after HFNC therapy. In the study conducted by Baudin et al., HFNC failure occurred in 22.0% of the participants.

In our study maximum failure rate of HFNC was observed in children with worsening respiratory disease with various underlying comorbidities which was 7 cases out of 12 (58.3%) and the remaining children with No underlying co morbidities which was 5 cases out of 12 (41.7%). However, this difference was not statistically significant. In the Chang et al., study the overall failure rate of HFNC therapy was 15.7%, with 16 out of 102 children escalated to other modes of ventilation.

Looking at association between HFNC status and age distribution of the study subjects, there was no significant association found between age group of children and HFNC status (p = 0.751). Similar results were obtained in the study conducted by Asseri et al., in which there was no significant association between age group and the HFNC status (p = 0.812).[13]

HFNC was successful in 22 out of 29 males (7.9%), with 7 failures (24.1%). Success was higher among females, with 26 out of 31 (83.9%) responding positively, and 5 failures (16.1%). But this difference in HFNC status with gender was not statistically significant. Asseri et al., also found similar results with no significant association between gender and HFNC status.[13]

Considering comorbidities, even though the HFNC failure rate was more among children with underlying co-morbidities, there was no significant association found between comorbidities and HFNC status. Contrary to our findings, in the study conducted by Asseri et al., there was significant association between HFNC status and comorbidities, with failure of HFNC seen more among individuals with history of associated chronic infections.[13]

No significant association was found between, indication for HFNC use and the success or failure of HFNC in our study. Same was the case in study conducted by Asseri et al., in which no significant association was found between the two variables.[13]

The mean FiO2 in the successful cases was 49.63%, compared to 54.83% in the HFNC failed cases. The difference was statistically significant with a P-value of 0.015. The maximum FiO2 was significantly higher in failed cases (64.58%) compared to successful cases (55.15%), with a P-value of <0.001. Similar findings were seen in the study conducted by Chang et al., in which there was significant difference in the FiO2 values as well as the max FiO2 values among the successful and failed cases of HFNC.[8]

There was no significant difference in flow rates between successful (28.42 L/min) and failed (29.25 L/min) cases, with a P-value of 0.654.

Similarly, there was no significant difference in the maximum flow rates between successful (42.94 L/min) and failed(40.75 L/min) cases, with a P-value of 0.643. But in the study conducted by Chang et al., both these values were found to be statistically significant.[8]

Patients who experienced HFNC failure had a significantly longer stay in the PICU (10.50 days) compared to those who had a successful HFNC therapy (6.13 days), with a P-value of 0.015. Similarly, the overall hospital stay was significantly longer for patients who failed HFNC therapy (14.75 days) compared to those who succeeded (12.69 days), with a P-value of <0.001. However, in the study conducted by Chang et al., no significant difference was found between both groups with respect to the stay in PICU and hospital.[8] While in the study conducted by Asseri et al., the duration of stay in PICU as well as the hospital was significantly different in both the groups.[13]

The average duration of HFNC therapy in our study was 56.50 ± 17.09 hours, indicating that most patients received HFNC therapy for a little over two days, with some variation in the duration of treatment across the study population. In the study conducted by Baudin et al., the median duration of HFNC therapy was 36 hours with interquartile range of 17 – 61 hours.[10] In the study conducted by Chang et al., the mean duration of HFNC use was 65.35 ± 75.45 hours. Thus, in most cases HFNC was found to be used for a period of 2 – 3 days, before the child got better or HFNC failed.[8]

The average length of stay in the PICU was 7.00 ± 2.39 days, indicating that most patients spent about a week in the PICU. The overall average hospital stay was 13.10 ± 2.61 days, suggesting that most patients remained hospitalised for nearly two weeks.

The mean SF ratio was found to be 215.37 ± 31.41 among the subjects who had a successful HFNC status, while it was 154.36 ± 36.58 among the subjects who had a failed HFNC status. This difference was statistically significant in our study.

In the study conducted by Chang et al. the SF ratio was 210.07 ± 41.72 among those who had a successful HFNC therapy and 147.43 ± 49.86 among those who had a failed HFNC therapy. Thus, a lower SF ratio is associated with development of failure of HFNC therapy.[8] Kamit et al., found that a lower SpO2/FiO2 (S/F) ratio at admission was indicative of failure in high-flow nasal cannula (HFNC). They also found that reaching a S/F ratio above 200 after 60 minutes strongly predicted successful HFNC treatment.[14]

At the end of the study, it was noted that there were 2 deaths (3.3%) among the study subjects, highlighting a small but significant mortality rate within this group. Mortality was attributed to worsening of Pneumonia and children with complications associated with mechanical ventilation.

In the study conducted by Asseri et al., the mortality rate was 9.8%, while the mortality rate in the study conducted by Chang et al., was 5.9%.[8] In the study conducted by Wing et al., the mortality rate was only 0.4%.[15]

CONCLUSION

The study concludes that HFNC therapy demonstrates an efficacy of 80% in children aged 2 months to 18 years who presented with acute respiratory distress with hypoxia.

Although 20% of patients required escalation to other non-invasive ventilation or endotracheal intubation, HFNC was generally effective as a first line treatment.

Age, gender did not significantly impact the failure rates of HFNC, but children with underlying medical conditions faced a higher risk of therapy failure, though this was not statistically significant. Furthermore patients experiencing HFNC failure had longer duration of stay at PICU as well as hospital. The SPO2/ FIO2 (S/F) ratio emerged as a potential predictor for the success or failure of HFNC therapy. Based on this findings HFNC can be considered a viable initial treatment option for children across all age groups with various causes of acute respiratory distress in paediatric intensive care unit.

Limitations:

1. There are no guidelines on escalation of HFNC to either non-invasive ventilation or intubation with mechanical ventilation in literature. Hence in our study the escalation was done based on clinical scenario and would have been different for different study participants. This would have affected the failure rate in our study.
2. Broader age groups and smaller sample size was one another limitation of our study.
3. Complications associated with HFNC use was not studied in detail due to the limited number of study participants.
4. This research was carried out at a single facility using a certain protocol that governs the use of HFNC, which restricts its external validity.

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