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High Flow Nasal Cannula as a Method for Rapid Weaning From Nasal Continuous Positive Airway Pressure

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ABSTRACT

Background: To compare two methods of weaning premature infants from nasal continuous positive airway pressure (NCPAP).

Methods: Between March and November 2012, 88 preterm infants who were stable on NCPAP of 5 cmH_2O with FIO_2 <30% for a minimum of 6 h were randomly allocated to one of two groups. The high flow nasal cannula (HFNC) group received HFNC with flow of 2 L/min and $FIO_2 = 0.3$ and then stepwise reduction of FIO_2 and then flow. The non-HFNC group was maintained on NCPAP of 5 cmH_2O and gradual reduction of oxygen until they were on $FIO_2 = 0.21$ for 6 h, and we had weaned them directly from NCPAP (with pressure of 5 cmH_2O) to room air.

Results: No significant differences were found between 2 study groups with regards to gestational age, birth weight, Apgar score at 1 and 5 min after birth, patent ductus arteriosus and use of xanthines. The mean duration of oxygen therapy after randomization was significantly lower in HFNC group compared to non-HFNC group (20.6 ± 16.8 h vs. 49.6 ± 25.3 h, $P < 0.001$). Also, the mean length of hospital stay was significantly lower in HFNC group compared to non-HFNC group (11.3 ± 7.8 days vs. 14.8 ± 8.6 days, $P = 0.04$). The rate of successful weaning was not statistically different between two groups.

Conclusions: Weaning from NCPAP to HFNC could decrease the duration of oxygen therapy and length of hospitalization in preterm infants.

Keywords: Continuous positive airway pressure, high flow nasal cannula, preterm infant, weaning

INTRODUCTION

Despite technological and clinical improvement in neonatal care, pulmonary disease is the most important cause of morbidity in premature neonates whose lungs are not fully developed. In the past decades, it was common to start endotracheal intubation and mechanical ventilation in newborns with moderate to severe respiratory problems.[1]

It has been well documented that endotracheal intubation and mechanical ventilation may lead to barotrauma, volutrauma, and endotrauma. In addition, intubation and mechanical ventilation could increase the risk of infection.[2,3]

The high incidence of pulmonary complications of mechanical ventilation has led to a tendency to use alternative methods of respiratory support in preterm infants.

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Nasal continuous positive airway pressure (NCPAP) is a noninvasive method that provides a constant positive pressure to the airways of spontaneously breathing infants. This constant pressure improves oxygenation by increasing functional residual capacity and recruitment of collapsed alveoli. In addition, NCPAP promotes redistribution of lung fluid and reduces upper airway resistance.[4] As a result, it is a useful and relatively safe method for treatment of respiratory problems especially in preterm infants.

Although NCPAP was primarily used for treatment of respiratory distress syndrome, it is a useful method for prevention of extubation failure and treatment of apnea of prematurity.[5-7]

Despite many documented benefits of NCPAP, it is a form of respiratory support that has its complications including traumatic injuries to the nose, pulmonary air leak syndromes and gaseous distension of the stomach.[8-10] Therefore, reducing the duration of NCPAP application could decrease the associated complications. However, premature discontinuation of NCPAP has potential hazards including increased apnea, oxygen demand and the need to restart NCPAP, and occasionally mechanical ventilation.

There is no consensus on the best method to wean from NCPAP. Many centers have used graded time off NCPAP to wean from NCPAP. It means removing NCPAP for a predefined number of hours each day (for example 4 h off and 20 h on) and step by step increasing the time off NCPAP every day pending NCPAP can be completely stopped, while the others gradually decrease the NCPAP pressure and FIO_2 during weaning.[11,12]

For several years, low flow nasal cannula (with flow rates of ≤1 L/min) has been used for delivering oxygen.[13] However, it has not provided significant respiratory support in newborn infants. Recently, some neonatologists have used a nasal cannula in premature newborns for weaning from NCPAP. High flow nasal cannula (HFNC) is defined as delivery of heated humidified and blended oxygen through the nasal cannula at flow rates of more than 1 L/min. This novel method could decrease airway water loss, airway cooling, thickened secretions and nasal irritation.[14,15]

The humidified HFNC system has been adopted as a primary support for respiratory distress syndrome,[16] for treating apnea of prematurity and to support premature neonates after extubation as an alternative to NCPAP. However, its efficacy for earlier weaning from NCPAP has not been well studied.

The objective of this study was to examine whether the use of HFNC with earlier discontinuation of NCPAP could decrease the duration of oxygen therapy and length of hospital stay in premature infants.

METHODS

Study design and participants

Between March and November 2012, we conducted a randomized controlled trial at the neonatal Intensive Care Unit (NICU) of Al-Zahra University Hospital, affiliated to Isfahan University of Medical Sciences, Isfahan, Iran. Inborn infants with gestational ages of 28–36 weeks who were met the following criteria were enrolled into the study: Receiving NCPAP at a pressure of 5 cmH_2O with FIO_2 requirement of 30% to maintain an oxygen saturation of 88–95%, the lack of apnea (pauses of respiration for more than 20 s associated with bradycardia or cyanosis with more than 2 episodes in 12 h or more than 3 episodes in 24 h with at least one which needed bag and mask ventilation)[17] or signs of respiratory distress including tachypnea, moderate or severe intercostal or subcostal retraction and nasal flaring under these NCPAP setting. Exclusion criteria were major congenital malformation, grade 3 or 4 intraventricular hemorrhage, neuromuscular disorders, pulmonary hypoplasia, cleft lip and palate, chest wall deformity, cyanotic congenital heart disease.

The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences. Parents of eligible newborns were approached for participation in the study, and informed consent was obtained from them.

Procedures and variable assessment

We have been used a uniform protocol for the management of respiratory distress syndrome in our NICU. Concisely, all newborns with spontaneous respiration that have signs of respiratory distress are placed on NCPAP with 5–6 cmH_2O. The continuous positive airway pressure (CPAP) pressure could increase up to 8 cmH_2O if respiratory distress is not alleviated. NCPAP failure is defined as increased work of breathing characterized by ongoing tachypnea (respiratory rate of more than 60 per min for more than 2 h), significant retraction, apnea as explained above, abnormal blood gases (2 samples with an interval of more than 2 h) with low pH of <7.2, PCO_2 of more than 65 mmHg and PaO_2 of <50 mmHg with FIO_2 of >60%).

Once the newborns remained stable for 6 h, we initiated NCPAP weaning. FIO_2 was lowered gradually down to 30%, then NCPAP pressure was reduced down to 5 cmH_2O.

The HFNC group was given HFNC with flow of 2 L/min and FIO_2 = 0.3 after discontinuation from NCPAP. FIO_2 were adjusted to maintain oxygen saturation between

88 and 95%. HFNC flow was kept at 2 L/min until FIO_2 requirements were 0.21. After that, we had lowered HFNC flow 0.5 L/min every 1 h until a flow of 0.5 L/min achieved. At this time, the infants were separated from HFNC. In the non-HFNC group the newborns were maintained on NCPAP and FIO_2 gradually decreased to 0.21. Patients stable on this setting for 6 h were weaned directly from NCPAP (with pressure of 5 cmH_2O) to room air. If their oxygen saturation has fallen below 88%, we have administered free flow oxygen by blender to achieve FIO_2 of 88–95. Successful weaning was defined as the absence of respiratory distress and no requirements of more than 0.21 for 72 h on room air. In the presence of any of the following conditions we applied NCPAP again in both groups: (1) The need for FIO_2 >60% to maintain oxygen saturation of more than 88%, (2) signs of respiratory distress including nasal flaring, retraction, tachypnea (respiratory rate of more than 70 for more than 1 h), (3) Apnea during first 48 h after discontinuation of NCPAP.

We recorded oxygen saturation and heart rate on Masimo Pulse Oxymeter (Masimo CO, Irvin, California, USA) during the study. We were used Bubble CPAP System (Fisher and Pykel Healthcare, Auckland, New Zealand) and short binasal cannula for NCPAP administration. HFNC system included a gas source, air/O_2 blender and a humidifier rendering air/O_2 via short nasal cannula (Fisher and Pykel RT329, Salter Labs).

We have started methylxanthines for treatment of apnea of prematurity on the basis of our NICU protocols. We have recorded newborn information including birth weight, gestational age, route of delivery, prenatal steroid use, prolonged rupture of membranes for more than 18 h before delivery, surfactant therapy. Presence of patent ductus arteriosus (PDA) and the need for methylxanthines.

Primary outcome

The main outcome was the duration of oxygen requirement.

Secondary outcomes

The secondary outcomes were duration of respiratory support, rate of successful weaning and duration of hospitalization.

Statistical analysis

Sample size calculation and data analysis

We calculated that a sample size of 41 infants in each group was needed to detect a difference of 30% for the duration of oxygen dependency with 80% power and significance of 0.05.

Randomization

Computer generated random numbers were used for randomization. Infants were randomized to one of two CPAP weaning groups from concealed envelopes opened by nonstudy personnel.

Blinding

The investigators in this trial were not blinded to study intervention.

Data were analyzed with the use of SPSS software (version 20, SPSS Inc., Chicago, IL, USA). Differences between groups were evaluated by Fischer's exact test and Chi-square for each categorical variable and by Student's *t*-test for each continuous variable.

RESULTS

A total of 109 preterm newborn with gestational ages of 28–36 weeks were recruited for the study. From these infants, 89 patients were enrolled in the trial and were randomized as shown in Figure 1. Of the 89 infants who enrolled the study, 88 newborns completed the study. We did not find any significant differences between 2 study groups with regards to gestational age, birth weight, route of delivery, Apgar score at 1 and 5 min after birth, PDA, use of xanthines, prolonged rupture of membranes and maternal pregnancy induced hypertension and prenatal steroid usage [Table 1]. There was no significant difference in the number of infants who successfully trailed off NCPAP in the first attempt between the HFNC group (3 infants) and non-HFNC group (2 infants) ($P = 0.8$). The infants were successfully weaned off supplemental oxygen at postconceptional ages of 36.5 ± 2.1 weeks in non-HFNC group and 33.2 ± 1.9 weeks in HFNC group [Figure 2]. The postconceptional age when the newborns came from respiratory support (NCPAP or HFNC) was not significantly different between HFNC group ($P = 0.8$). The mean duration of oxygen therapy was significantly lower in HFNC group compared to non-HFNC group (20.6 ± 16.8 h vs. 49.6 ± 25.3 h, $P < 0.001$). Also, the mean length of hospital stay was significantly lower in HFNC group compared to non-HFNC group (11.3 ± 7.8 days vs. 14.8 ± 8.6 days, $P = 0.04$).

Table 1: Baseline characteristics of the study population

	Non-HFNC group (n=44)	HFNC group (n=44)	P
Male sex (%)	27 (61.4)	27 (61.4)	0.29
GA (weeks)±SD	31.6±2.5	31.2±2.6	0.25
Birth weight (g)±SD	1830±653	1867±470	0.3
Caesarean delivery (%)	39 (88.6)	40 (90.9)	0.36
Maternal PIH (%)	15 (34.1)	10 (22.7)	0.12
PROM (%)	14 (31.8)	10 (22.7)	0.17
Apgar score at 1 min±SD	5±1	5±0.8	1
Apgar score at 5 min±SD	8±1.2	7±2.4	0.1
Maternal perinatal steroid (%)	16 (36.4)	14 (31.8)	0.33
Patent ductus arteriosus (%)	13 (29.5)	12 (27.3)	0.41
Use of xanthines (%)	11 (25)	16 (36.4)	0.12
Surfactant (%)	27 (62.7)	24 (54.5)	0.22

SD=Standard deviation, HFNC=High flow nasal cannula, GA=Gestational age, PROM=Premature rupture of membranes, PIH=Pregnancy-induced hypertension

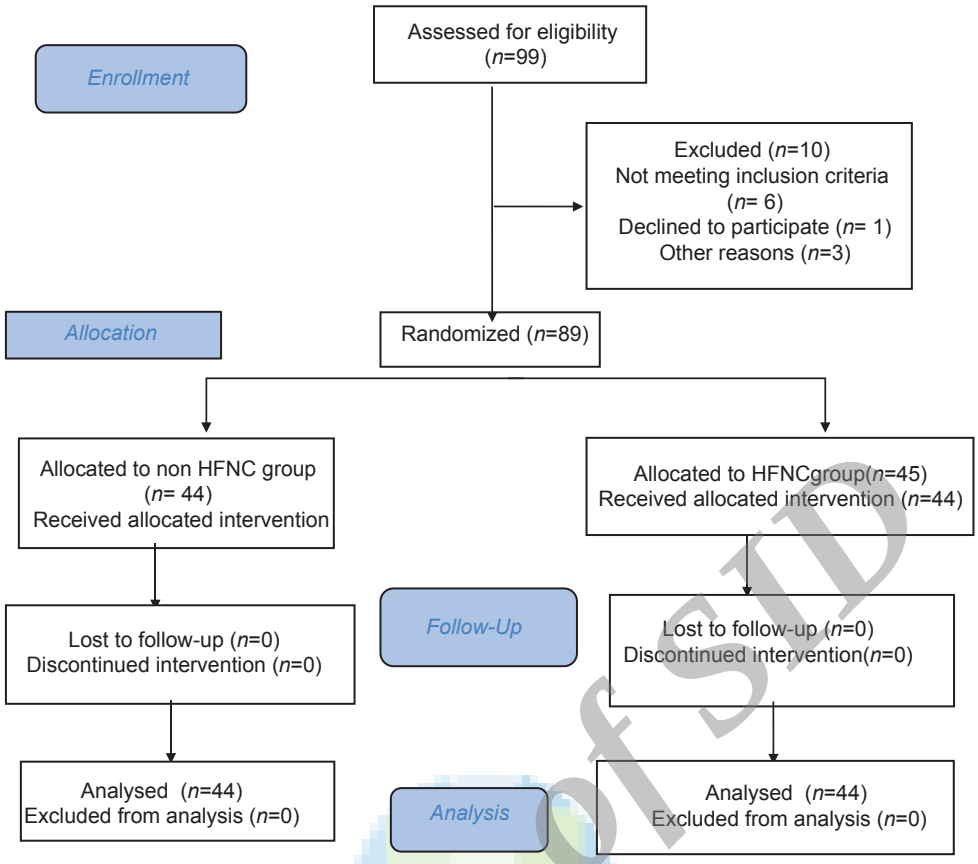

Figure 1:The study flow

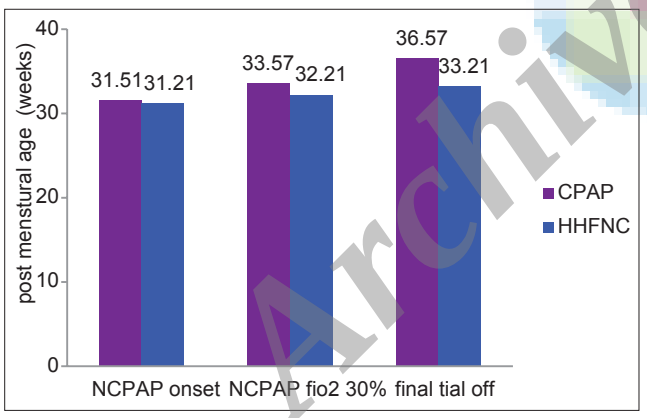

Figure 2: Comparison of two groups based on postmenstrual age at: Continuous positive airway pressure onset, FiO2 of 30% and final trial off

Eleven infants (25%) in the non-HFNC group and 17 infants (38.6%) in the HFNC had significant apnea, (P = 0.12) and received methylxanthines.

Four neonates (9.1%) in the nonHFNC group required mechanical ventilation because of respiratory failure, but no infant in HFNC group required mechanical ventilation (P = 0.05). Outcome indicators of both groups are represented in Table 2.

DISCUSSION

We were trying to find a method for faster weaning from NCPAP in premature infants. Our study has shown an average of 12 h decrease in the duration of oxygen therapy and a 3.5 days decrease in the length of hospital stay in newborns weaned prematurely from NCPAP to HFNC.

Singh *et al*. conducted a study on 112 premature infants who were stable on NCPAP and needed <0.3 FIO_2. They used two methods for weaning from NCPAP. The first method included gradual lowering of CPAP pressure to a predetermined level of pressure and the second method included stepwise increasing duration of time off NCPAP. They found that the median time on NCPAP was significantly lower in the first group. The mean number of days on NCPAP in the pressure group was 1.5 days that is very close to our results.[11]

Soe *et al*. compared the success rate of two weaning methods of decreasing airway pressure and graded time off from NCPAP in preterm newborns and found that successful weaning was significantly higher in the pressure group.[12]

Although we did not use the graded time off method, we also found that gradual decreasing of NCPAP pressure to

Table 2: Outcome indicators in both groups

	Non-HFNC group (n=44)	HFNC group (n=44)	P
Intraventricular hemorrhage grade 3 or 4 (%)	2 (4.5)	0	0.12
Necrotizing enterocolitis (%)	1 (2.3)	0	0.25
Sepsis (%)	21 (48.8)	17 (38.6)	0.09
Need for mechanical ventilation (%)	4 (9.1)	0 (0)	0.056
Bronchopulmonary dysplasia (%)	1 (2.3)	3 (6.8)	0.16
Postmenstural age at FiO_2=30%±SD	33.57±3.1	32.21±2.8	0.16
Need to restart CPAP (%)	2 (4.5)	3 (6.8)	0.8
Hours of oxygen therapy±SD	49.6±3.8	20.6±2.5	0.01
Length of hospital stay±SD	14.8±1.30	11.3±1.26	0.04

SD=Standard deviation, HFNC=High flow nasal cannula, CPAP=Continuous positive airway pressure

a predetermined level of pressure is a very useful method for weaning from NCPAP.

Todd and Associates randomized 154 preterm newborns to one of the three methods of NCPAP weaning: Rapid discontinuation of NCPAP, graded time off without using nasal cannula and graded time off using nasal cannula. They found that infants in the first method group had significantly shorter duration of weaning period and length of hospital stay.[18] Although we did not use a graded time off method, the rapid discontinuation of NCPAP in this study is very similar to non-HFNC method in our study. However, the mean duration of oxygen therapy using rapid discontinuation of NCPAP was about 24 days that is much longer than the figure of 2 days in our study of the non-HFNC group. This difference is probably due to lower gestational ages of newborns enrolled in Todd's study. Because more premature infants have lower lung compliance and a longer time is needed to reach normal lung compliance. In addition, bronchopulmonary dysplasia is more likely to develop in more premature infants.

Abdel-Hady *et al*. conducted a study to find the better approach for weaning preterm infants from NCPAP and found that weaning off directly from a pressure of 5 cmH_2O and FIO_2 of = 21% to room air could significantly decrease duration of oxygen therapy in comparison to using HFNC (2 L/min) after discontinuation of NCPAP with a pressure of 5 cmH_2O and FIO_2 of ≤30%. However, the length of hospitalization and other outcomes did not differ significantly between two groups.[19]

In contrast, our study revealed that the mean duration of oxygen therapy was significantly lower in HFNC group compared to non-HFNC group. Also, the mean length of hospital stay was significantly lower in HFNC group compared to non-HFNC group. These differences may be due to differences in methodology. The mean duration of oxygen therapy in non-HFNC group in our study was about 2 days compared to 5 days in that study. This difference could partially be due to shorter maintenance on NCPAP after initial stabilization in our study (6 h instead of 24 h). Moreover, they were kept flow rate at 2 L/min until the FIO_2 requirements were 0.21and then the HFNC flow was lowered step by step by 0.5 L/min every 6 h until a flow of 0.5 L/min was attained. We also did not lower flow rate until the FIO_2 requirements were 0.21 but, the HFNC flow was decreased gradually 0.5 L/min every 1 h until a flow of 0.5 L/min was attained. So it seems that using the most similar methods could yield more similar results.

We found that the need for intubation and mechanical ventilation was higher in newborns who enrolled in the non-HFNC group but, this difference was not significant. We speculated that this difference may be due to higher number of infants suffered from severe intraventricular hemorrhage in non-HFNC group.

Recently, Rastogi *et al*. conducted a study to compare rapid (sudden cessation of NCPAP when infants were stable for 48 h on NCPAP of 5 cmH_2O and FIO_2 of = 21% to room air) and gradual (cycling off for 3 h alternating with cycling on for 3 h for 48 h) weaning from NCPAP in infants <32 weeks gestation. They did not find significant differences between groups with regards to the success rate of initial weaning, length of hospital stay and postmenstural age at time of weaning from supplemental oxygen and concluded that factors other than CPAP weaning method, such as maturity of the lungs may affect the success of NCPAP weaning in premature newborns.[20]

We also found that successful weaning was not significantly different between two groups.

To the best of our knowledge and belief, this study is the first on NCPAP weaning method that used such aggressive timetable and producing such promising results. However, our study had some limitations. First of all blinding of care providers was not possible because of the nature of the study using two different devices for respiratory support. Secondly, although we defined the success and failure of the weaning methods by clinical guidelines, it is likely that subjectivity of the care providers' decision could affect the final results.

CONCLUSIONS

Weaning premature infants off NCPAP could successfully be done by HFNC or by decreasing FIO_2 to 21% after reaching NCPAP pressure of 5 cmH_2O. HFNC can decrease the duration of oxygen therapy and length of hospital stay.

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