

A Comparison of Humidified High Flow Nasal Cannula with Bubble CPAP in Very Low Birth Weight Infants

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ABSTRACT

Purpose: To compare the effect of humidified high flow nasal cannula (HHFNC) with that of nasal continuous positive airway pressure (NCPAP) as the mode of extubation in very low birth weight infants (VLBWI).

Methods: Medical records were retrospectively reviewed for 219 VLBWI who were admitted to the neonatal intensive care unit of Ajou University Hospital from January 2009 through December 2012; 87 were supported by noninvasive ventilation (NIV) after extubation (HHFNC n=47, NCPAP n=40). Extubation failure was defined as the need for reintubation within 1 week of extubation.

Results: (1) There were no significant differences between the groups in demographic data such as gestational age, birth weight, and age at extubation. (2) There were no significant differences in fraction of inspired oxygen (FiO₂) (HHFNC 0.23±0.03 vs. NCPAP 0.23±0.03, *P*-value .937) and peak inspiratory pressure (HHFNC 11±6.6 cmH₂O vs. NCPAP 10.3±3.4 cmH₂O, *P*-value .559) before extubation. (3) The rate of extubation failure and FiO₂ values after extubation were similar in the 2 groups (extubation failure, HHFNC 5/47 vs. NCPAP 5/40, *P*-value 1.000; FiO₂, HHFNC 0.24±0.05 vs. NCPAP 0.25±0.04, *P*-value .399). (4) Among patients who received NIV after extubation once but did not receive further intubation, the duration of NIV or duration of oxygen supply were not significantly different between the groups (NIV, HHFNC 12.4±9.1 days vs. NCPAP 8.7±12.3 days, *P*-value .159, oxygen supply, HHFNC 49.0±40.3 days vs. NCPAP 50.9±41.3 days, *P*-value .844) or bronchopulmonary dysplasia rate (HHFNC 24.3% vs. NCPAP 34.4%, *P*-value .430).

Conclusion: HHFNC is as effective as NCPAP for weaning VLBWIs from invasive mechanical ventilation.

Key Words: Noninvasive ventilation, Bronchopulmonary dysplasia, Preterm infants, Endotracheal extubation

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INTRODUCTION

Invasive mechanical ventilation is used to treat respiratory distress syndrome (RDS) in preterm infants. However, noninvasive ventilation (NIV) methods such as nasal continuous positive airway pressure (NCPAP) are preferred over invasive methods in order to protect the lungs of preterm infants; a correlation exists between the duration of mechanical ventilation and the development of bronchopulmonary dysplasia (BPD)¹⁻³. NCPAP has been widely used as an effective NIV modality and is associated with a number of important physiological benefits, including stabilization of the airways, increased lung volume, decreased airway resistance, and reduced work of breathing^{4,5}. Nonetheless, NCPAP has its disadvantages: it requires a relatively bulky interface, which can lead to problems involving maintenance of its proper position and predisposition to nasal irritation and trauma^{6,7}.

In recent years, humidified high flow nasal cannula (HHFNC) therapy has become widely used. HHFNC is increasingly popular as a supportive modality in situations where NCPAP might traditionally have been used. The popularity of HHFNC over NCPAP is at least partly due to HHFNC's greater ease of use, as well as reports of its improved tolerability and greater efficacy⁸⁻¹¹. Although the frequency of HHFNC use has increased, few studies have compared its efficacy with that of NCPAP. Therefore, we compared the effects of NCPAP and HHFNC as modes of extubation in very low birth weight infants (VLBWI).

MATERIALS AND METHODS

1. Study design & data collection

We retrospectively reviewed the medical records of all VLBWIs admitted to the neonatal intensive care unit (NICU) of Ajou University Hospital from January 2009 to December 2012. Only the first NIV event was reviewed for patients who experienced multiple NIV events. For each HHFNC and NCPAP event, we compared demographic data such as gestational age (GA), birth weight, Apgar score, fraction of antenatal steroid use and methylxanthine use, existence of operated retinopathy of prematurity (ROP), patent ductus arteriosus (PDA) treated by ibuprofen or surgery, necrotizing enterocolitis (NEC) stage 2 or greater, intraventricular hemorrhage (IVH) grade 3 or greater, and pneumothorax. We also compared variables before extubation such as body weight at extubation, age at extubation, pre-extubation fraction of inspired oxygen (FiO₂),

and pre-extubation peak inspiratory pressure (PIP). We also compared outcomes such as extubation failure rate and post-extubation FiO₂.

We used bubble NCPAP as the NIV modality for patients with RDS before 2011. However, many nasal septum irritation events were reported during CPAP use; therefore, we used HHFNC as the primary NIV modality instead of bubble NCPAP since January 2011.

NCPAP support was provided using bubble CPAP (Fisher & Paykel Healthcare Inc., New Zealand) utilizing pressure ranging from 4 to 8 cmH₂O. HHFNC was generated by an MR 850 heated humidifier (Fisher & Paykel Healthcare Inc., New Zealand) at flow rates of 2-8 L/min.

Reintubation was performed in patients who had uncompensated respiratory acidosis with a pH of <7.25 and an FiO₂ requirement of >0.6 to maintain a transcutaneous saturation of >90%, those with severe apnea (defined as apnea and bradycardia requiring bag and mask ventilation or reintubation), and those with frequent apnea (defined as ≥3 apnea events of any severity within 1 hour).

2. Statistics & definitions

SPSS ver. 19.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Demographics, variables associated with pulmonary conditions and outcomes were compared between the 2 groups using Student's t-test and Fisher's exact test. Categorical data are presented as percentage (%), and continuous data are presented as mean±(SD) or median (25-75 percentile). A *P*-value <0.05 was considered statistically significant.

This study was approved by the Institutional Review Board of Ajou University Hospital.

BPD was defined as an ongoing requirement for supplemental oxygen at 36 weeks corrected GA¹². The classification of NEC stage was based on the modified Bell's staging criteria¹³ and the classification of IVH was based on the criteria provided in the report of Papile et al.¹⁴. Extubation failure was defined as the requirement for reintubation within 1 week of extubation.

RESULTS

1. Comparisons of demographics and variables associated with pulmonary conditions before extubation

Fig. 1 shows the patient scheme of our study of 219 VLBWIs in the NICU of Ajou University Hospital from January 2009 to

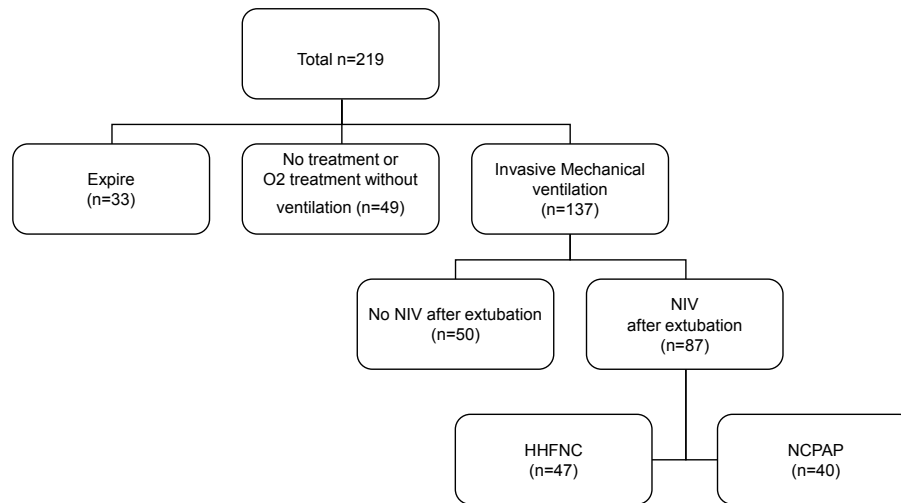


Fig. 1. The scheme of the study population. Abbreviations: NIV, noninvasive ventilation; HHFNC, humidified high flow nasal cannula; NCPAP, nasal continuous positive airway pressure.

Table 1. Comparisons of Demographic Data of HHFNC and NCPAP

	HHFNC (n=47)	NCPAP (n=40)	P-value
Gestational age(wks)*	28 ⁺¹ ±2 ⁺²	28 ⁺⁰ ±2 ⁺³	.773
Birth weight(gram)*	1,077±210	1,041±210	.423
Apgar score 1 min [†]	4 [3-5]	3 [2-4.5]	.068
Apgar score 5 min [†]	6 [5-6]	5 [3-5.5]	.002
Antenatal steroid (n/%)	37/78.7	24/60.0	.065
Methylxanthine (n/%)	46/97.9	39/97.5	1.000
Theophylline (n/%)	17/36.2	39/97.5	
Caffeine (n/%)	29/61.7	0/0	
PDA (n/%)	31/66.0	23/57.5	.507
Operated ROP (n/%)	3/6.4	4/10.0	.698
IVH ≥ grade III (n/%)	4/8.5	1/2.5	.369
NEC ≥ stage IIa (n/%)	2/4.3	5/12.5	.240
Pneumothorax (n/%)	3/6.4	3/7.5	1.000
Nasal septum injury (n/%)	2/4.3	5/12.5	.159

*expressed as mean±SD.

[†]expressed as median [25%-75%].

Abbreviations: HHFNC, humidified high flow nasal cannula; NCPAP, nasal continuous positive airway pressure; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis.

December 2012. Of 219 VLBWIs, 87 infants received the NIV after extubation. Out of 87 infants, 47 were provided with HHFNC, and 40 were provided with NCPAP.

There were no significant differences between the HHFNC and NCPAP groups in demographic data such as GA, birth weight, antenatal steroid use, methylxanthine use, PDA treated by ibuprofen

Table 2. Comparisons of Variables Associated with Pulmonary Conditions before Extubation

	HHFNC (n=47)	NCPAP (n=40)	P-value
Body weight at extubation (g)*	1,265±406	1,230±458	.710
Age at extubation (weeks)*	30 ⁺⁵ ±3 ⁺²	30 ⁺⁵ ±3 ⁺³	.918
Pre extubation FiO ₂ (%)*	0.23±0.03	0.23±0.03	.937
Pre extubation PIP (%)*	11.0±6.6	10.3±3.4	.559

*expressed as mean±SD.

Abbreviations: HHFNC, humidified high flow nasal cannula; NCPAP, nasal continuous positive airway pressure; FiO₂, fraction of inspired oxygen; PIP, peak inspiratory pressure.

or surgery, operated ROP, IVH grade 3 or greater, NEC stage 2 or greater, BPD, and pneumothorax. However, there were significant differences in Apgar score at 5 min between the HHFNC and NCPAP groups (Table 1).

There were no significant differences between the groups in body weight at extubation, age at extubation, FiO₂ and PIP before extubation (Table 2).

2. Comparison of extubation failure rates and variables associated with pulmonary condition after extubation

The extubation failure rates and FiO₂ values after extubation were not statistically significantly different between the HHFNC and NCPAP groups (Table 3).

Among patients who received NIV after extubation once but did not receive further intubation, there were no differences between the HHFNC and NCPAP groups in the duration of NIV, duration of

Table 3. Comparison of Extubation Failure Rates and Variables Associated with Pulmonary Conditions after Extubation

	HHFNC (n=47)	NCPAP (n=40)	P-value
Extubation failure (n/%)	5/10.6	6/12.5	1.000
Post extubation FiO ₂ *	0.24±0.05	0.25±0.04	.399

*expressed as mean±SD.

Abbreviations: HHFNC, humidified high flow nasal cannula; NCPAP, nasal continuous positive airway pressure; FiO₂, fraction of inspired oxygen.

Table 4. Comparison of Durations of NIV or Oxygen Supply

	HHFNC (n=37)	NCPAP (n=32)	P-value
Duration of NIV (day)*	12.4±9.1	8.7±12.3	.159
Duration of oxygen supply (day)*	49.0±40.3	50.9±41.3	.844
BPD (n/%)	9/24.3	11/34.4	.430

*expressed as mean±SD.

Abbreviations: HHFNC, humidified high flow nasal cannula; NCPAP, nasal continuous positive airway pressure; NIV, noninvasive ventilation; BPD, bronchopulmonary dysplasia.

oxygen supply, and BPD rate (Table 4).

DISCUSSION

In our study, there were no significant differences in variables such as body weight at extubation, age at extubation, pre-extubation FiO₂ and pre-extubation PIP between the HHFNC and NCPAP groups. In addition, there were no statistically significant differences in the rates of extubation failure, post-extubation FiO₂ values, duration of NIV, duration of oxygen supply, and BPD rate between the HHFNC and NCPAP groups. Other studies have compared the efficacy of HHFNC with that of NCPAP¹⁵⁻¹⁸⁾, but few studies have focused on the efficacy of HHFNC and NCPAP as weaning strategies in VLBWIs.

Shoemaker et al.¹⁵⁾ found no differences in demographic data between patients provided with NCPAP and those provided with HHFNC; they also found that more infants were intubated due to early NCPAP failure than early HHFNC failure (40% vs. 18%). There study showed that HHFNC was well tolerated and effective as an alternative respiratory support mode. However, the infants who received HHFNC or NCPAP had either been enrolled immediately after admission for an escalation of support from oxyhood or low-flow nasal cannula, or enrolled immediately following extubation from mechanical ventilation within 96 hours of birth. Demographic

data such as GA and birth weight were not significantly different between the groups; however, in contrast to our study, their study focused on the efficacy of HHFNC as an NIV modality in neonatal respiratory disease, not its efficacy as a weaning modality after extubation.

Holleman-Duray et al.¹⁶⁾ enrolled preterm infants of 25 to 29 weeks' GA who received an early extubation protocol. They divided the infants into the HHFNC group and a control group. The control group received NCPAP, nasal cannula oxygen inhalation or room air. They reported that the groups did not differ in pulmonary outcomes and adverse outcomes, and that infants in the HHFNC group were extubated from a higher ventilator rate and spent fewer days on the ventilator. Additionally, their study compared the duration of parenteral nutrition, the number of days to reach full feed, the length of stay, and weight at discharge, and no significant differences were found in these parameters between the HHFNC and control groups. However, HHFNC was not compared with NCPAP in that study, and therefore, it is of limited value for comparing the efficacies of HHFNC and NCPAP as weaning methods from invasive mechanical ventilation.

Campbell et al.¹⁷⁾ studied preterm infants with birth weights <1,250 g; in their study, infants were randomized either to CPAP generated via a high flow cannula (infant size, Salter Labs, Arvin, CA, USA) or the Infant Flow Nasal CPAP System (VIASYS, Conshohocken, PA, USA) at extubation. They reported that high flow CPAP was associated with a higher rate of reintubation and increased oxygen use, along with a higher incidence of apnea and post-extubation bradycardia. The demographic data of their enrolled infants were similar to those in our study, but there were differences in the high flow CPAP device used and the flow rates via the high flow cannula. Their high flow CPAP device consisted of a nonheated bubble humidifier that provided lower flow rates (L/min) using the formula (flow=0.92+0.68x, x=weight in kg), while our high flow CPAP device consisted of a heated humidifier providing approximately 4-8 L/min via a nasal cannula.

Yoon et al.¹⁸⁾ conducted a retrospective study of preterm infants of 25-30 weeks GA; infants were divided into HHFNC and NCPAP subgroups. They selected only NCPAP data (n=17) during the first period of the study and only HHFNC data (n=34) during the second period. As for our study, they reported no significant differences in demographic data between the NCPAP and HHFNC groups, and no significant differences in outcomes such as extubation failure rate, BPD rate, and duration of oxygen or NIV supply. Yoon et al. concluded that HHFNC is an effective NIV modality,

but their study was limited in its applicability due to the potential for historical bias and a small sample size.

In our study, there were no significant differences in demographic data such as GA, birth weight, antenatal steroids and methylxanthine use, existence of PDA treated by ibuprofen or surgery, operated ROP, IVH grade 3 or greater, NEC stage 2 or greater, and pneumothorax between the HHFNC and NCPAP groups (although Apgar score at 5 min did significantly differ between the groups). Although the 5-min Apgar score in the HHFNC group was higher than that in the NCPAP group in our study, there were no significant differences in long-term outcomes such as IVH, NEC, and BPD between the HHFNC and NCPAP groups, and therefore, we were able to exclude the influence of Apgar score on post-extubation variables.

In conclusion, HHFNC is helpful as an extubation weaning modality, and furthermore, HHFNC did not prolong the duration of NIV or oxygen supply. Therefore, we conclude that HHFNC is as effective as NCPAP as a method for weaning VLBWIs from invasive mechanical ventilation.

There are some limitations to our study. First, this study was retrospective; therefore, the possibility of randomization bias does exist. However, there were no differences in demographic data and variables associated with pulmonary conditions before extubation. Second, this study may have been subject to historical bias in the selection of NIV modalities; however, there were no differences in demographic data and treatment policies between the 2 periods. Third, we investigated only 219 VLBWIs over 4 years; therefore, randomized prospective trials and larger studies are needed in the future.

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극소 저체중 출생아에서 경비지속기도양압과 가슴고유량비강캐놀라의 사용에 관한 비교연구

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목적: 극소저체중출생아에서 발관 시 가슴고유량비강캐놀라와 경비지속기도양압의 효과에 대해 비교연구 하였다.

방법: 2009년 1월부터 2012년 12월까지 아주대학교병원 신생아집중치료실에 입원한 출생체중 1,500 g 미만 환아들을 의무기록을 중심으로 후향적 분석하였다.

결과: 가슴고유량비강캐놀라와 경비지속기도양압군 간에 (1) 제태연령, 출생체중, 발관 시 나이 등의 통계 값, (2) FiO_2 , PIP, (3) 발관실패율 및 발관 후 FiO_2 , (4) 비침습적 환기의 기간, 산소투여 기간, 기관지폐이형성증 발병률에서 차이가 없었다.

결론: 가슴고유량비강캐놀라는 극소저체중출생아에서 침습적 기계환기로부터 발관하는 데 있어 경비지속기도양압만큼 효과적이다.