IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Original Article

Heated Humidified High-Flow Nasal Cannula Versus Nasal Continuous Positive Airway Pressure for the Facilitation of Extubation in Preterm Neonates with Respiratory Distress

Kalyan Chakravarthy Konda*, Leslie Edward Lewis, Ramesh Bhat Y, Jayashree Purkayastha, Shravan Kanaparthi

Department of Paediatrics, Kasturba Medical College, Manipal, Manipal University, Karnataka, India

ABSTRACT

Background: Heated humidified high-flow nasal cannula (HHHFNC) is gaining popularity as an alternative to nasal continuous positive airway pressure (nCPAP) therapy in the management of preterm neonates with respiratory distress due to ease of administration and patient comfort. However, limited evidence is available addressing its risks and benefits. To study the efficacy and safety of HHHFNC in comparison to nCPAP for the facilitation of extubation in preterm neonates (born at 27-34 weeks of gestation) with respiratory distress.

Methods: A prospective observational study was conducted, where 64 neonates were assigned either to nCPAP (n=34) or HHHFNC (n=30) groups post-extubation. The primary outcome was treatment failure (defined by pre-specified criteria) requiring a higher modality of respiratory support within 72 hours after extubation.

***Results*:** Treatment failure was seen in 36.7% of neonates assigned to the HHHFNC group compared to 14.7% in the nCPAP group (P=0.043). The incidence and severity of nasal trauma were higher in the nCPAP group compared to the HHHFNC group (nCPAP: 58.6% vs. HHHFNC: 15.7%; P=0.001). No significant difference was observed between the two groups in terms of other outcomes such as days on primary non-invasive ventilation (NIV), days of total NIV, duration of hospitalization, days to reach full enteral feeding, weight gain at discharge, incidence and severity of nasal trauma, incidence of pneumothorax, necrotizing enterocolitis, intraventricular hemorrhage, retinopathy of prematurity, sepsis, and death.

Conclusion: Though a gentler modality with less incidence of nasal trauma, HHHFNC does not appear to be as effective as nCPAP in the management of preterms with respiratory distress.

Keywords: CPAP, HHHFNC, Preterm neonates, Respiratory distress syndrome

Introduction

Respiratory distress syndrome (RDS) is the major etiology of respiratory morbidity in preterm neonates. Though invasive ventilation (with surfactant administration) forms the cornerstone of the management, it is a double-edged sword with potential concerns of development of ventilator-associated lung injury (VALI), bronchopulmonary dysplasia (BPD), infection, and airway trauma (1). The tidal volumes and pressures generated by invasive ventilation coupled with the inflammatory insult account for volutrauma, barotrauma, and biotrauma, respectively, and all of them contribute to lung injury individually as well as collectively (2, 3). In view of the above-stated concerns associated with prolonged invasive ventilation, change has set in favoring the usage of non-invasive ventilation (NIV).

NIV is used post-extubation to assist the neonate in smooth respiration and to prevent

* *Corresponding author*: Kalyan Chakravarthy Konda, Department of Paediatrics, Kasturba Medical College, Manipal, Manipal University, Karnataka, India. Tel: +919902191336; Email: k.kalyan.22189@gmail.com

Please cite this paper as:
Chakravarthy Konda K, Edward Lewis L, Bhat YR, Purkayastha J, Kanaparthi Sh. Heated Humidified High-Flow Nasal Cannula Versus Nasal Continuous Positive Airway Pressure for the Facilitation of Extubation in Preterm Neonates with Respiratory Distress. Iranian Journal of Neonatology. 2018 Jun: 9(2). DOI: 10.22038/ijn.2017.24517.1314

extubation failure. With advances in antenatal and perinatal care, trend attempts to use NIV as an alternative modality to invasive ventilation to manage the smallest of the babies with respiratory distress avoiding intubation. Though superiority of NIV over invasive ventilation remains questionable, NIV is still considered a safe and effective modality when used properly.

Continuous positive airway pressure (CPAP) refers to the application of positive pressure to the airway of a spontaneously breathing infant throughout the respiratory cycle.The pressure delivered by CPAP is well measured and regulated (4). It acts through preventing the collapse of the alveoli, stabilization of the chest wall, increasing functional residual capacity (FRC), and improving ventilation-perfusion (V/Q) mismatch (5, 6). It has been shown to reduce extubation failure, treat apnea and respiratory distress syndrome, and reduce chronic lung disease by minimizing the duration of mechanical ventilation (7). It remains the current standard, widely accepted, and time-tested modality of NIV. However, its limitations include bulky interface, complicated fixation technique, poor patient tolerance, and nasal trauma (8).

The above issues led to the advent of a newer modality of NIV named heated humidified high-flow nasal cannula (HHHFNC), which has gained popularity given its perceived benefits of ease of administration, user- and baby-friendly interface, and less nasal trauma. Further, the establishment of feeding and Kangaroo mother care can be early, easy, and comfortable with this technique (9–11).

HHHFNC delivers heated (to body temperature, i.e., 37°C) and humidified (near 100% relative humidity) gas at flow rates of more than 1 l/min through small bi-nasal prongs (12). The major drawback of HHHFNC is that the positive airway pressure generated by it is neither measurable nor regulated warranting its use in neonates with caution (13–16). The present study aimed at determining the efficacy and adverse effects of HHHFNC (a new and user-friendly modality) in comparison to nasal continuous positive airway pressure (nCPAP; the current standard of NIV), post-extubation, in preterm neonates with respiratory distress syndrome.

Methods

We conducted a prospective observational study that was approved by the Institutional Ethics Committee (IEC No 656/2014), from November 2014 to September 2016 at a level III neonatal intensive care unit (NICU). Preterm neonates born between 27-34 weeks of gestational age were included in the study if they met all of the following criteria: a) greater than 750 g birth weight, b) received invasive ventilation within 24 hours of birth, and c) required non-invasive respiratory support (either nCPAP or HHHFNC) post-extubation. Outborn neonates were included if transferred to the study center within 24 hours of life and satisfied the inclusion criteria. The exclusion criteria included abnormalities of the upper and lower airway, congenital intestinal anomalies, major congenital heart diseases, chromosomal abnormalities, other major congenital defects, occurrence of death or pneumothorax before extubation, and neonates discharged against medical advice.

Neonates were assigned to two groups based on their gestational age (27-30 weeks and 31-34 weeks). In each gestational age group, the subjects were assigned to either modality of NIV post-extubation by quasi experimental allocation. In case the proposed modality of treatment could not be used due to the limitation of resources, they were assigned to the other available modality. The neonates received surfactant as per unit protocol whenever indicated and feasible. It was either early rescue surfactant therapy (ERST; surfactant administration within 2 hours of birth) or late rescue surfactant therapy (LRST; surfactant administration ≥ 2 hours after birth) (17).

All the neonates received caffeine 6 hours before extubation. A trial of extubation was considered if the neonate had spontaneous respiratory effort, stable hemodynamic parameters, and the following ventilator parameters were met: fraction of inspired air (FiO_2) < 30%, peak inspiratory pressure (PIP) ≤ 14 cm of water, and respiratory rate (RR) < 34/min. Treatment failure was defined as one or more of the following criteria (18–21): a) persistent or marked severe retractions with distress, b) FiO_2 requirement > 50% to maintain the target oxygen saturation, c) more than one apneic episode requiring intermittent positive pressure ventilation within a 6-hour period, d) six or more apneic episodes requiring stimulation within 6 consecutive hours, and e) pH of less than 7.2 and a partial pressure of CO_2 > 60 mmHg on arterial blood gas analysis. Neonates in the HHHFNC group were permitted to be switched over to nCPAP in case of HHHFNC failure. However, neonates failing nCPAP were not considered for a trial of

HHHFNC during acute respiratory distress. Infants failing either intervention were managed with non-synchronized nasal intermittent mandatory ventilation (NIMV) or re-intubation and synchronized intermittent mandatory ventilation (SIMV).

Nasal CPAP support was provided with a ventilator (Drager baby log 8000, Germany) or underwater bubble system (Fischer and Paykel, New Zealand) using a nasal mask as an interface. Neonates were extubated to the peak end expiratory pressure (PEEP) value equivalent to that on ventilator support and FiO_2 5% higher the value of what was being used before extubation. The maximum PEEP allowed was 6 cm H_2O. HHHFNC was delivered using a healthcare kit with RT350 humidifier (Fischer and Paykel, New Zealand) or Airvo (Fischer and Paykel, New Zealand) using nasal cannula. The neonates were extubated to a flow rate of 8 l/min and FiO_2 5% higher the value of what was being used before extubation. The flow rate was weaned to a minimum of 2 l/min before discontinuing support. The FiO_2 was adjusted to maintain the target oxygen saturation as per center protocol.

The primary outcome was treatment failure of the NIV within 72 hours of initiation of support, which signified the need for a change of treatment modality. The other outcome measured was days on primary NIV. Primary NIV is the modality of NIV to which the neonates were immediately assigned to following extubation. The outcome, days on primary NIV (measures the number of days the neonate required the primary modality of NIV before the baby could tolerate weaning from respiratory support for at least 24 continuous hours), days of total NIV (total NIV support required during hospital stay, till discharge, it may be HHHFNC/nCPAP/HHHFNC+nCPAP), duration of hospitalization (days to reach full enteral feeding [120 ml/kg/day]), weight gain at discharge (g/kg/day), incidence and severity of nasal trauma (as per classification of the decubitus lesions from the US NPUAP)(22), incidence of pneumothorax, necrotizing enterocolitis (NEC; based on modified Bell's staging criteria) (23), severe intraventricular hemorrhage (IVH; grade ≥3 according to Papile grading) (24), retinopathy of prematurity (ROP; as per the International Committee for Classification of ROP)(23), culture-positive sepsis, and death.

Statistical analysis was performed using SPSS, version 20. To compare the outcome variables on a continuous scale two-sample t-test or Mann Whitney U test were used as appropriate. To compare the outcome variables on nominal type of data, Chi-square test or Fisher's Exact test were run as appropriate. P-values less than 0.05 were considered statistically significant.

Results

During the study period, 179 neonates were born (or admitted to our NICU on day 1 in case of outborn) between 27-34 weeks of gestation. Overall, 115 neonates were excluded due to various reasons (Figure 1).

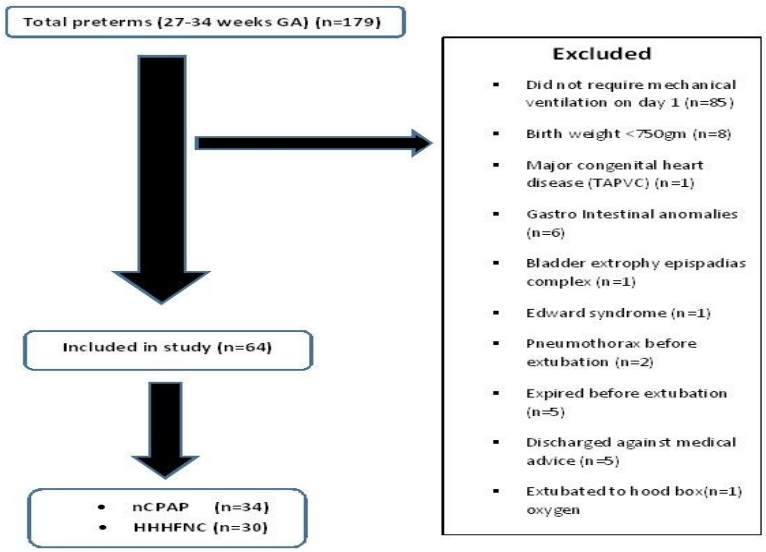

Figure 1. Flow diagram of the study population

Table 1. Baseline characteristics of the neonates

Characteristics	nCPAP (n=34)	HHHFNC (n=30)
Male n(%)	17(50%)	16(53.3%)
Inborn n(%)	27(79.4%)	25(83.3%)
Birth weight (g) Mean ± SD	1130 ± 235	1135 ± 240
Gestational age (weeks) Mean ± SD	30 ± 1.6	29.6 ± 1.7
Growth status at birth n (%)		
SGA	9(26.5%)	2(6.7%)
AGA	25(73.5%)	28(93.3%)
Maternal age (years) Mean ± SD	28.8 ± 4.5	28 ± 3.4
Primipara mother n(%)	12(35.3%)	15(50%)
Antenatal corticosteroids received n(%)	21(61.8%)	21(70%)
Vaginal delivery n(%)	7(20.6%)	5(16.7%)
Delivery room intubation n(%)	9(26.5%)	10(33.3%)
APGAR at 1min* Median(IQR25th-75th)	7(5-8)	6(4-8)
APGAR at 5 min† Median(IQR25th-75th)	9(8-9)	9(7-9)
Surfactant – n (%)‡	33(97.1%)	28(93.3%)
ERST – n (%)	23(69.7%)	24(85.7%)
LRST – n(%)	10(30.3%)	4(14.3%)
Hours of mechanical ventilation prior to extubation median (IQR25th–75th)	39 (20-70)	35 (22-58)

*- APGAR details were available only for 52 neonates (CPAP- 27/34, HFNC-25/30)
†- Babies intubated at birth were excluded
‡- 33/34 neonates in CPAP group and 28/30 neonates in HHHFNC group only received surfactant therapy.
SGA: small for gestational age,
AGA: appropriate for gestational age
nCPAP: nasal continuous positive airway pressure
HHHFNC: heated humidified high-flow nasal cannula

Table 2. Treatment failure on NIV (primary outcome)

Outcome	nCPAP (n=34)	HHHFNC (n=30)	P-value
Treatment failure (within 72 h after initiation of primary modality of NIV) n (%)	5(14.7%)	11(36.7%)	0.043(S)
Reason for treatment failure			
Respiratory distress (n)	3	9	
Apnea (n)	2	2	
Support upgraded to (after failure)			
nCPAP (n)	-	10	
NIMV (n)	3	-	
SIMV (n)	2	1	
Required re-intubation (within 72 h after initiation of primary modality of NIV) n	5 (3+2)	5 (4+1)	

nCPAP: nasal continuous positive airway pressure
HHHFNC: heated humidified high-flow nasal cannula

Out of the 64 neonates who participated in the study, 34 were assigned to the nCPAP group and 30 to the HHHFNC group.

No significant difference was observed between the two groups regarding their baseline characteristics like gender, mean birth weight, mean gestational age, antenatal steroids administration in mother, and mode of delivery making them comparable to one another (Table 1).

The primary outcome (Table 2), treatment failure requiring switching over to a higher modality of respiratory support, occurred in 5 out of 34 (14.7%) neonates in the nCPAP group and 11 out of 30 (36.7%) neonates in the HHHFNC group, which was statistically significant (P=0.043).

The higher incidence of nasal trauma (Table 3) was observed in the CPAP group (58.6%) in comparison to the HHHFNC group (15.7%) with a significant *P*-value (P=0.001). No significant difference was observed in other outcomes between the two treatment groups in the current study (Table 3).

Table 3. Secondary outcomes

Outcome	nCPAP (n=34)	HHHFNC (n=30)	P-value
Days on primary NIV* Median(IQR25th-75th)	9.2(5-13.5)	11(8-16)	0.219
Total days on NIV†			
Median (IQR25th-75th)	11(5.7-17.5)	12(8.5-34)	0.243
Range (Max-Min)	57-2	41-6	
Day of initiation of enteral feeding Median(IQR25th-75th)	2(2-3)	2.5(2-3)	0.571
Days required to reach full enteral feeding‡ Median(IQR25th-75th)	11(7-12)	12(9-14)	0.241
Days of hospitalization† Mean (± SD)	42.81 (± 15.49)	42.38 (± 16.69)	0.928
Weight(g) at discharge† Mean (± SD)	1735.38 (± 121.10)	1679.52 (±118.61)	0.119
Weight gain (g/kg/day) during hospital stay† median (IQR25th-75th)	10.6 (7.9-16.6)	9.7 (5.9-14.5)	0.303
Nasal trauma§ n (%)	17(58.6%)	3(15.7%)	0.001(S)
Grade I (Erythema) (n)	12	3	
Grade II (Superficial ulcer) (n)	3	-	
Grade III (Necrosis) (n)	2	-	
Death n(%)	8(23.5%)	9(30%)	0.559
Pneumothorax (n)	-	-	
Intraventricular hemorrhage n (%)	1	2	
Periventricular leukomalacia (n)	-	-	
Necrotizing enterocolitis n(%)	9(26.5%)	10(33.3%)	0.549
Stage I	6	4	
Stage II	1	3	
Stage III	2	3	
Sepsis n(%)	12(35.3%)	14(46.7%)	0.335
Retinopathy of prematurity† n (%)	6(23%)	4(19%)	0.924
Requiring laser photocoagulation (n)	2	0	

NIV: non-invasive ventilation
nCPAP: nasal continuous positive airway pressure
HHHFNC: heated humidified high-flow nasal cannula
*- Neonates who failed primary modality of NIV and neonates who expired before discharge were not included. (CPAP n=25, HFNC n=15)
†- Neonates who expired before discharge were not included. (CPAP n=26, HFNC n=21)
‡- Neonates who never reached 120ml/kg/day enteral feeds were excluded. (CPAP n=26, HFNC-22)
§- Neonates who were switched from one form of NIV to another were excluded in the analysis of nasal trauma. (CPAP n=29, HHHFNC n=19). Few neonates were switched from nCPAP to HHHFNC therapy due to miscellaneous causes like need for the CPAP unit for another baby, etc. This change of NIV was only after resolution of acute respiratory distress and not to be confused with treatment failure of CPAP

Discussion

In the present study, treatment failure (primary outcome) was significantly more in the HHHFNC group. A similar observation (nCPAP: 4 vs. HHHFNC: 14) was noted in a study by Kadivar et al. (25). However, in other similar studies (19–21, 26), treatment failure rate between the two groups showed no significant statistical difference. In the current study, the most common reason for treatment failure was persisting or worsening respiratory distress on the primary modality of NIV, which was similar to the observations made by Yoder et al. (20) and Soonsawad et al. (26).

Nonetheless, in a study by Manley et al. (19), the most common reason for failure was apnea. In the present study, all the 5 (100%) babies who failed nCPAP required re-intubation within 72 h. However, out of the 11 babies who failed HHHFNC, only 5 (45%) required re-intubation, and the remaining 6 (55%) babies were successfully managed with nCPAP and avoided re-intubation. In a similar study by Manley et al. (19), 38/39 (97.4%) babies who failed CPAP required re-intubation (1 baby was successfully managed with NIMV), and in the HHHFNC group 27/52 (52%) babies required re-intubation, while the remaining 25/52 (48%) were successfully managed with CPAP and NIMV.

In the current study, duration of primary NIV support (median, nCPAP: 9.2 vs. HHHFNC: 11) and total NIV support (median, nCPAP: 11 vs. HHHFNC: 12) were less in the nCPAP group in comparison to the HHHFNC group; however, P-value remained to be insignificant (Table 3). In a study by Yoder et al. (20), the durations of primary NIV and total NIV support were significantly less in the CPAP group compared to the HHHFNC group. Nevertheless, in a study by Shoemaker et al. (18), ventilator days per patient were less in the HHHFNC group when compared to the CPAP group (HHHFNC: 9.9 vs. CPAP: 19.4).

The significantly higher incidence of nasal trauma was observed in the nCPAP group in the present study (Table 3). In the nCPAP group, two neonates developed grade III nasal trauma requiring change of NIV to HHHFNC. None in the

HHHFNC group developed ulceration of the skin/mucosa. In other similar studies, the incidence of nasal trauma was significantly high in CPAP group (19–21, 26). In a study by Collins et al. (21), 20% of neonates assigned to CPAP were switched to HHHFNC as a result of nasal trauma. In a study by Manley et al. (19), many neonates in the HHHFNC group developed nasal injury, and they were transferred to receive other forms of NIV like CPAP. The difference was more significant if the diagnosis of nasal trauma was limited to cases that were diagnosed during the assigned primary treatment.

The major concern with the use of HHHFNC is unregulated pressure generation, which might cause air leak syndromes. Studies by Saslow et al. (27), Kubicka et al. (28), and Wilkinson et al. (29) showed that the pressure generated by HHHFNC was milder and never exceeded 6 cm of water and was sufficient enough to produce positive clinical effects. In the current study, though we did not directly measure airway or pharyngeal pressure, no baby on HHHFNC therapy developed air leak or pneumothorax. No statistical significance was observed in other outcomes in the current study, which was in line with the results obtained by other similar studies (19–21, 25, 26).

We acknowledge the following limitations to our study: small sample size, and crossover bias (restriction of switching over from nCPAP to HHHFNC in case of treatment failure, however, permitting the vice versa), though a bias, it reflects the practical and ethical aspects of clinical practice around the world at centers where both treatments are available. It also helped to limit the financial burden for patients. The results of our study pertain only to neonates for the facilitation of extubation and should not be extrapolated to the use of HHHFNC as a primary mode of respiratory support after birth.

Conclusion

According to the results, HHHFNC therapy is not as effective as nCPAP therapy for the facilitation of extubation in preterm neonates as evident from the higher treatment failure rate in the former group. The incidence and severity of nasal trauma were higher in the nCPAP group compared to the HHHFNC group highlighting HHHFNC as a gentler, more comfortable, and kinder approach. There is a need for larger clinical trials to assess its clinical utility and establish the standard of care outweighing benefits and risks.

Acknowledgments

None.

Conflicts of interests

None.

References

1. Coalson JJ. Pathology of new bronchopulmonary dysplasia. Semin Neonatol. 2003; 8(1):73-81.
2. Whitehead T, Slutsky AS. The pulmonary physician in critical care-7: ventilator induced lung injury. Thorax. 2002; 57(7):635-42.
3. Van Marter LJ, Allred EN, Pagano M, Sanocka U, Parad R, Moore M, et al. Do clinical markers of barotrauma and oxygen toxicity explain interhospital variation in rates of chronic lung disease? The Neonatology Committee for the Developmental Network. Pediatrics. 2000; 105(6):1194-201.
4. De Paoli AG, Davis PG, Faber B, Morley CJ. Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates. Cochrane Database Syst Rev. 2008; 1:CD002977.
5. Courtney SE, Pyon KH, Saslow JG, Arnold GK, Pandit PB, Habib RH. Lung recruitment and breathing pattern during variable versus continuous flow nasal continuous positive airway pressure in premature infants: an evaluation of three devices. Pediatrics. 2001; 107(2):304-8.
6. Richardson CP, Jung AL. Effects of continuous positive airway pressure on pulmonary function and blood gases of infants with respiratory distress syndrome. Pediatr Res. 1978; 12(7):771-4.
7. De Paoli AG, Morley C, Davis PG. Nasal CPAP for neonates: what do we know in 2003? Arch Dis Child Fetal Neonatal Ed. 2003; 88(3):F168-72.
8. Loftus BC, Ahn J, Haddad J Jr. Neonatal nasal deformities secondary to nasal continuous positive airway pressure. Laryngoscope. 1994; 104(8 Pt 1):1019-22.
9. Chao KY, Chen YL, Tsai LY, Chien YH, Mu SC. The role of heated humidified high-flow nasal cannula as noninvasive respiratory support in neonates. Pediatr Neonatol. 2017; 58(4):295-302.
10. Hough JL, Shearman AD, Jardine LA, Davies MW. Humidified high flow nasal cannulae: current practice in Australasian nurseries, a survey. J Paediatr Child Health. 2012; 48(2):106-13.
11. Manley BJ, Owen L, Doyle LW, Davis PG. High-flow nasal cannulae and nasal continuous positive airway pressure use in non-tertiary special care nurseries in Australia and New Zealand. J Paediatr Child Health. 2012; 48(1):16-21.
12. Wilkinson D, Andersen C, O'Donnell CP, De Paoli AG, Manley BJ. High flow nasal cannula for respiratory support in preterm infants. Cochrane Database Syst Rev. 2016; 2:CD006405.
13. Locke RG, Wolfson MR, Shaffer TH, Rubenstein SD, Greenspan JS. Inadvertent administration of positive

end-distending pressure during nasal cannula flow. Pediatrics. 1993; 91(1):135-8.
14. Chang GY, Cox CC, Shaffer TH. Nasal cannula, CPAP and vapotherm: effect of flow on temperature, humidity, pressure and resistance. Pediatr Acad Soc. 2005; 57:1231.
15. Sreenan C, Lemke RP, Hudson-Mason A, Osiovich H. High-flow nasal cannulae in the management of apnea of prematurity: a comparison with conventional nasal continuous positive airway pressure. Pediatrics. 2001; 107(5):1081-3.
16. Frey B, Shann F. Oxygen administration in infants. Arch Dis Child Fetal Neonatal Ed. 2003; 88(2):F84-8.
17. Polin RA, Carlo WA; Committee on Fetus and Newborn; American Academy of Pediatrics. Surfactant replacement therapy for preterm and term neonates with respiratory distress. Pediatrics. 2014; 133(1):156-63.
18. Shoemaker MT, Pierce MR, Yoder BA, DiGeronimo RJ. High flow nasal cannula versus nasal CPAP for neonatal respiratory disease: a retrospective study. J Perinatol. 2007; 27(2):85-91.
19. Manley BJ, Owen LS, Doyle LW, Andersen CC, Cartwright DW, Pritchard MA, et al. High-flow nasal cannulae in very preterm infants after extubation. N Engl J Med. 2013; 369(15):1425-33.
20. Yoder BA, Stoddard RA, Li M, King J, Dirnberger DR, Abbasi S. Heated, humidified high-flow nasal cannula versus nasal CPAP for respiratory support in neonates. Pediatrics. 2013; 131(5):e1482-90.
21. Collins CL, Holberton JR, Barfield C, Davis PG. A randomized controlled trial to compare heated humidified high-flow nasal cannulae with nasal continuous positive airway pressure postextubation in premature infants. J Pediatr. 2013; 162(5):949-54.
22. Fischer C, Bertelle V, Hohlfeld J, Forcada-guex M, Stadelmann-Diaw C, Tolsa J. Nasal trauma due to continuous positive airway pressure in neonates. Arch Dis Child Fetal Neonatal Ed. 2010; 95(6):F447-51.
23. Cloherty JP, Eichenwald EC, Stark AR. Manual of neonatal care. Philadelphia: Lippincott Williams & Wilkins; 2012.
24. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1500 gm. J Pediatr. 1978; 92(4):529-34.
25. Kadivar M, Mosayebi Z, Razi N, Nariman S, Sangsari R. High flow nasal cannulae versus nasal continuous positive airway pressure in neonates with respiratory distress syndrome managed with INSURE method: a randomized clinical trial. Iran J Med Sci. 2016; 41(6):494-500.
26. Soonsawad S, Swatesutipun B, Limrungsikul A, Nuntnarumit P. Heated humidified high-flow nasal cannula for prevention of extubation failure in preterm infants. Indian J Pediatr. 2017; 84(4):262-6.
27. Saslow JG, Aghai ZH, Nakhla TA, Hart JJ, Lawrysh R, Stahl GE, et al. Work of breathing using high-flow nasal cannula in preterm infants. J Perinatol. 2006; 26(8):476-80.
28. Bouaram BA, Fernandes CJ. Heated, humidified high-flow nasal cannula therapy: yet another way to deliver continuous positive airway pressure? Pediatrics. 2008; 121(1):218-9.
29. Wilkinson DJ, Andersen CC, Smith K, Holberton J. Pharyngeal pressure with high-flow nasal cannulae in premature infants. J Perinatol. 2008; 28(1):42-7.