Jornal de Pediatria 2024;100(2): 212—217

Jornal de Pediatria
www.jped.com.br

ORIGINAL ARTICLE

Comparison of the effectiveness of different high-flow devices in neonatal care☆

Diogo Machado Kaminski [a,*], **Graziela Ferreira Biazus** [a], **Rita C. Silveira** [b], **Renato Soibelmann Procianoy** [b]

[a] *Hospital de Clínicas de Porto Alegre, Department of Physiotherapy, Neonatology Service, Porto Alegre, RS, Brazil*
[b] *Newborn Section at Universidade Federal do Rio Grande do Sul, Hospital de Clínicas de Porto Alegre, Neonatology Service, Porto Alegre, RS, Brazil*

Received 26 July 2023; accepted 17 October 2023
Available online 27 November 2023

KEYWORDS
Newborn;
Preterm;
Respiratory distress;
Non-invasive ventilation;
Extubation;
High-flow nasal cannula

Abstract

Objective: To evaluate the success rate of high-flow nasal cannula (HFNC) therapy using an adapted obsolete mechanical ventilator (MV), Optiflow™ and Vapotherm™ in newborns (NBs).
Method: This was a retrospective observational study conducted in the neonatal intensive care unit (NICU). The sample comprised NBs who underwent HFNC therapy due to ventilatory dysfunction, for weaning from non-invasive ventilation (NIV), or post-extubation. The three groups, stratified according to gestational age (GA) and birth weight, and corrected GA and weight at the beginning of HFNC use, were as follows: Optiflow ™, Vapotherm ™, and obsolete Mechanical Ventilator (MV) adapted for high flow therapy. Subsequently, the NBs were divided into a success group (SG) and a failure group (FG). HFNC success was defined as a therapy duration exceeding 72 h.
Results: A total of 209 NBs were evaluated, with 31.1 % using HFNC due to ventilatory dysfunction, 2.4 % after extubation, and 66.5 % after NIV weaning. HFNC success rate was observed in 90.9 % of the NBs, with no difference between equipment types (Vapotherm ™, Optiflow ™, and adapted VM).
Conclusion: Different types of HFNC equipment are equally effective when used in neonatology for respiratory dysfunction, as a method of weaning from NIV and post-extubation. Adapted obsolete MV can be an alternative for HFCN therapy in resource-constrained settings.

Introduction

High-flow nasal cannula (HFNC) or high-flow oxygen therapy is a non-invasive ventilatory support that delivers a humidified and heated medical gas mixture with a flow rate that

☆ Service and Institution: The Neonatal Intensive Care — HCPA.

* Corresponding author.
E-mail: dkaminski@hcpa.edu.br (D.M. Kaminski).

https://doi.org/10.1016/j.jped.2023.10.006

exceeds the patient's spontaneous inspiratory flow.[1] Since its implementation, initially to treat apnea of prematurity,[2] HFNC therapy has expanded in a variety of clinical situations, becoming increasingly popular in Neonatal Intensive Care Units (NICU).[3]

Like traditional methods of non-invasive ventilation (NIV), such as nasal intermittent positive pressure ventilation (IPPV) or continuous positive airway pressure (CPAP), HFNC may prevent extubation failure in preterm infants with respiratory distress syndrome (RDS),[4-6] thereby reducing the risk of complications such as Bronchopulmonary Dysplasia, sepsis, neurological injury, and retinopathy of prematurity.[7] Additionally, HFNC has emerged as a strategy for weaning from NIV[8-11] and as a primary ventilatory support in preterm infants.[12-14] However, to ensure its efficacy and safety in preterm infants with different gestational ages and clinical conditions, further studies are needed.[12-18]

HFNC is generally considered for newborns (NBs) who exhibit signs of tachypnea, increased ventilatory work, oxygen requirements, and the need for continuous ventilatory support, similar to traditional NIV methods.[15] Its preference is attributed to the simplicity of installation and equipment handling, greater comfort, and reduced rate of nasal injury.[4,11,13,15,17,18]

The most commercially known devices for delivering high-flow therapy to NBs are Optiflow ™ (Fisher & Paykel MR850 (FP) and Vapotherm 2000i™ (VT). Although each HFNC system has its own particularities, these devices have the capacity to deliver heated and humidified flow, providing effects similar to the extubation success of infants born between 26 and 29 weeks.[19] While HFNC has been increasingly used in neonatology, there is uncertainty regarding whether or not HFNC can be considered cost-effective. It was demonstrated, that as the sole primary support for respiratory distress of NBs, CPAP is the dominant strategy and is more effective and on average cheaper than HFNC.[20]

In hospital and health services with limited financial resources, and lacking specific HFNC equipment, or modern mechanical ventilators (MV), using an adapted obsolete MV to function as a flow generator can be a viable and equivalent alternative for incorporating HFNC therapy as a modality of ventilatory support in NBs. Therefore, the aim of this study is to evaluate the success rate of HFNC with different equipment in NBs with ventilatory dysfunction, as well as its use in optimizing NIV weaning and post-extubation therapy.

Materials and methods

This was a retrospective observational study in which the clinicians were blinded to the type of device used in therapy with HFNC. It was carried out in the level III Neonatal Intensive Care Unit (NICU) of a public hospital, which serves as a reference center for high-risk pregnancies and high-risk newborns, with a capacity of 20 intensive care beds. The study was approved by the Research Ethics Committee of the Institution under number 4.508.659 and followed the principles established in Resolution No. 466 of 2012 of the National Health Council. During the process of submitting the project to the ethics and research committee, the researchers signed the Term of Commitment for Use of Data, guaranteeing the confidentiality and anonymity of the data of the participants and evaluators.

The primary outcome of this study was to evaluate the success rate of HFNC with different equipment in NBs with ventilatory dysfunction, as well as its use in optimizing NIV weaning and post-extubation therapy. The sample consisted of NBs who were treated with HFNC therapy from January 2018 to December 2022. The NBs were divided into three groups based on the type of HFNC equipment used: an adapted obsolete MV, Vapotherm™, and Optiflow™. HFNC parameters were recorded at the beginning and end of therapy. Clinical and demographic characteristics, HFNC indication, and the outcome of interest were evaluated. The decision to choose the high-flow device was based on convenience, depending on its availability in the NICU.

NBs were stratified into three categories according to prematurity at birth and the corrected gestational age at the beginning of HFNC: NBs $\leq$ 32 weeks (very and extremely premature), NBs between 32 and $<$ 37 weeks (moderately premature), and NBs $\geq$ 37 weeks (term). Similarly, NBs were divided based on birth weight and weight at the beginning of HFNC: NBs $<$ 2000 g or NBs $\geq$ 2000 g.

Subsequently, the NBs were classified into a Success Group (SG) and a Failure Group (FG). HFNC success was defined as a therapy duration exceeding 72 h. FG was characterized by ventilatory dysfunction, respiratory acidosis, partial pressure of carbon dioxide greater than 60 mm Hg, and more than one episode of apnea (respiratory pause $>$ 20 s and bradycardia), needing NIV or mechanical ventilation.

HFNC was indicated for NBs with ventilatory dysfunction, for weaning from NIV, or post-extubation. Ventilatory dysfunction was determined by a change in the ventilatory pattern or work, manifested by tachypnea, apnea, expiratory moan, stridor, chest retraction, nose flaring, or any sign of respiratory distress requiring ventilatory support. The group included NBs who were previously stable and had already discontinued some ventilatory support, such as mechanical ventilation, NIV, or even HFNC. Weaning from NIV to HFNC was performed in NBs with difficulty in weaning or those with nasal lesions due to the interface. Post-extubation, HFNC was initiated for NBs who were extubated from mechanical ventilation directly to HFNC. Preterm NBs $\leq$ 32 weeks received intravenous caffeine since the first 24 h of life, preterm NBs 32 and $<$ 37 weeks in the 24 h before extubation and during hospital stay if they presented apnea.

The HFNC-specific device used included Optiflow ™ (Fisher & Paykel Healthcare, New Zealand) and Vapotherm ™ (Vapotherm Inc., USA). An obsolete MV (Newport Wave E-200, USA) was adapted for high-flow nasal cannula oxygen delivery. This one has a basic and related simple setup, an air-oxygen blender allowed regulate FIO2 from 0.21 to 1.0 and generates up to 8 L/min flow. The gas was heated and humidified through an active-heated humidifier (MR850, Fisher & Paykel Healthcare) and delivered via a single-limb heated inspiratory circuit. The NBs breathed adequately heated and humidified medical gas through the specifics of high-flow nasal cannulas.

All three devices delivered heated and humidified medicinal gas mixtures (oxygen + compressed air) with adjustable flow rates and FiO2. A previously developed protocol was used for all NBs. The initial flow rate was set above 2 L/min,

Table 1 Characteristics of the newborns treated with HFNC with MV adapted, Vapotherm™ and Optiflow™.

	MV adapted (*n* = 53)	Vapotherm ™ (*n* = 39)	Optiflow ™ (*n* = 117)	Total (*n* = 209)	p-value
Demographic characteristics n (%)					
Male gender	35 (66)	21 (53.8)	62 (53)	118 (56.5)	0.265 [a]
GA birth (weeks)					0.333 [a]
< 32 weeks	41 (77.4)	29 (74.4)	78 (66.7)	148 (70.8)	
32 to < 37 weeks	7 (13.2)	6 (15.4)	15 (12.8)	28 (13.4)	
≥ 37 weeks	5 (9.4)	4 (10.3)	24 (20.5)	33 (15.8)	
Birth weight (grams)					0.102 [a]
< 2000	46 (86.8)	30 (76.9)	84 (71.8)	160 (76.6)	
≥ 2000	7 (13.2)	9 (23.1)	33 (28.2)	49 (23.4)	
GA (weeks) - start of HFNC					0.410 [a]
< 32 weeks	13 (24.5)	11 (28.2)	41 (35)	65 (31.1)	
32 to < 37 weeks	26 (49.1)	21 (53.8)	46 (39.3)	93 (44.5)	
≥ 37 weeks	14 (26.4)	7 (17.9)	30 (25.6)	51(24.4)	
HFNC start weight (grams)					0.259 [a]
< 2000	34 (64.2)	31 (79.5)	79 (67.5)	144 (68.9)	
≥ 2000	19 (35.8)	8 (20.5)	38 (32.5)	65 (31.1)	
Clinical manifestations n (%)					
RDS	45 (84.9)	30 (76.9)	95 (81.2)	170 (81.3)	0.623 [a]
Pulmonary hypertension	8 (15.1)	10 (25.6)	12 (10.3)	30 (14.4)	0.059 [a]
PDA	32 (60.4)	20 (51.3)	45(38.5)	97 (46.4)	0.023 [a]
PIVH	20 (37.7)	18 (46.2)	44 (37.6)	82 (39.2)	0.618 [a]
corticoid postnatal	24 (45.3)	7 (17.9)	29 (24.8)	60 (28.7)	0.006 [a]
Indication for HFNC n (%)					0.243 [a]
Ventilatory dysfunction	12 (22.6)	13 (33.3)	40 (34.2)	65 (31.1)	
Post-extubation	3 (5.7)	1 (2.6)	1 (0.9)	5 (2.4)	
NIV weaning	38 (71.7)	25 (64.1)	76 (65)	139 (66.5)	
HFNC data					
Initial flow - average (SD)	5.9 ± 1	6.1 ± 1	5.6 ± 1	5.8 ± 1	0.055 [b]
Initial flow Kg/L - average (SD)	3.6 ± 2	4 ± 2	3.6 ± 2	3.7 ± 3	0.459 [b]
Final flow - average (SD)	3.8 ± 1	4.5 ± 2	4.2 ± 2	4.1 ± 2	0.037 [b]
Final flow Kg/L - average (SD)	2.3 ± 1	2.9 ± 2	2.7 ± 2	2.7 ± 1	0.086 [b]
Initial FiO2- median	0.22	0.25	0.25	0.24	0.318 [b]
Final FiO2- median	0.21	0.21	0.21	0.22	0.438 [b]
HFNC period (days)	9 (4;13)	7 (4;14)	6 (6;12)	7 (3;13)	0.110 [b]
HFNC failure < 72 h	3 (5.7)	1 (2.6)	15 (12.5)	19 (9.1)	0.094 [a]

GA (gestational age); RDS (Respiratory Distress Syndrome); HFNC (High Flow Nasal Cannula); NIV (Non-Invasive Ventilation); PDA (persistent ductus arteriosus); PIVH (peri-intraventricular hemorrhage); SD (Standard Deviation); Kg/L (kilograms liters).

[a] Chi-square.

[b] Kruskal -Wallis test.

and it was increased by 0.5 L/min based on clinical conditions and work of breathing, up to a maximum of 8 L/min. FiO2 was adjusted according to the patient's SpO2 target. Flow rates and FiO2 were periodically evaluated, and HFNC weaning was initiated based on clinical stability, with the flow rate gradually reduced to a minimum of 2 L/min. Treatment could be stopped when FiO2 remained below 0.3 for more than 24 h. NBs who failed HFNC therapy were transitioned to NIV or mechanical ventilation. Nasal interfaces used were the BC425 model (Fisher & Paykel Healthcare, Auckland, New Zealand), Optiflow nasal prong ™ (Fisher & Paykel Healthcare, Auckland, New Zealand), and slender nasal cannula (Vapotherm Inc., USA). Any of the three cannula models were used for the adapted ventilator (Newport Wave E-200, USA). Infants were fitted with prongs that maintained a leak at the nose, with the aim of occluding approximately half the nares.

Statistical analysis was performed using SPSS software (Statistical Package for Social Science) version 29. Descriptive analysis of categorical variables was expressed as n (% of all patients), and continuous variables were presented as mean and standard deviation or median and interquartile range, depending on their distribution (normal or asymmetric, respectively). A comparison of the HFNC success rate and other categorical variables between the devices was conducted using the chi-square test (p-value < 0.05). For continuous variables, the Kruskal-Wallis test or Analysis of Variance (ANOVA) was utilized (p-value < 0.05).

Results

A total of 209 NBs were included in the study, with 53 NBs using the adapted obsolete MV, 39 using Vapotherm™, and 117 using Optiflow™. Among them, 66 % were male, 70.8 % had a GA at birth < 32 weeks and 70.6 % had a weight < 2000 g. Considering the corrected GA at the beginning of HFNC, 31.1 % of the NBs were in the range of < 32 weeks and 44.5 % had 32 weeks to < 37 weeks. It was observed that 77.6 % of the NBs weighed < 2000 g at the start of HFNC therapy. The group of NBs using Optiflow ™ had a higher number of PDA and postnatal corticosteroid therapies (p = 0.006). Among the NBs, 31.1 % used HFNC due to ventilatory dysfunction, while 2.4 % and 66.5 % used it after extubation and NIV weaning, respectively. The initial average

Table 2 Gestational age at birth and at the beginning of HFNC, clinical manifestations and indication of HFNC in SG and FG.

	SG (*n* = 190)	FG (*n* = 19)	p-value
GA birth n (%)			0.023 [a]
< 32 weeks	139 (93.9)	9 (6.1)	
32 to < 37 weeks	25 (89.3)	3 (10.7)	
≥ 37 weeks	26 (78.8)	7 (21.2)	
GA at the beginning of HFNC n (%)			0.117 [a]
< 32 weeks	62 (95.4)	3 (4.6)	
32 to < 37 weeks	85 (91.4)	8 (8.6)	
≥ 37 weeks	43 (84.3)	8 (15.7)	
Clinical manifestations n (%)			
Respiratory Distress Syndrome	157 (92.4)	13 (7.6)	0.130 [a]
Pulmonary hypertension	28 (93.3)	2 (6.7)	0.618 [a]
PDA	90 (92.8)	7 (7.2)	0.380 [a]
PIVH	77 (93.9)	5 (6.1)	0.226 [a]
Corticoid therapy	57 (95.0)	3 (5.0)	0.192 [a]
Indication for HFNC n (%)			0.685 [a]
Ventilatory dysfunction	58 (89.2)	7 (10.8)	
Post-extubation	5 (100.0)	0	
NIV weaning	127 (91.4)	12 (8.9)	

SG (Success Group); FG (Failure Group); HFNC (High Flow Nasal Cannula); GA (gestational age); NIV (Non-Invasive Ventilation); PDA (persistent ductus arteriosus); PIVH (Peri-intraventricular hemorrhage).
[a] Chi-Square.

flow was 5.8 L/min, and Optiflow ™ had a lower flow compared to the adapted VM and Vapotherm ™. The final HFNC flow averaged 4.1 L/min, with the adapted MV having the lowest flow value in relation to Vapotherm ™ and Optiflow ™, respectively (p = 0.037). The initial FIO2 and final FIO2 are not different between groups. There was no difference among equipment types regarding the number of days of HFNC therapy (Table 1).

The SG was composed of 190 NBs, while the FG had 19 NBs. The HFNC failure rate was 6.1 % for NBs with GA < 32 weeks, 10.7 % for those between 32 and < 37 weeks, and 21.2 % for NBs ≥ 37 weeks (p = 0.023). GA at the beginning of HFNC therapy did not show a difference (p = 0.117). Additionally, clinical manifestations and indications for HFNC were not different between SG and FG (Table 2)

Of the 19 NBs with HFNC failure < 72 h, 74 % used NIV as a rescue method, and 26 % used mechanical ventilation. In the group that used HFNC for weaning from NIV, 58 % of the NBs used NIV (CPAP or IPPV) as rescue, and 5 % used mechanical ventilation. Among the NBs who underwent HFNC after ventilatory dysfunction, 21 % switched to mechanical ventilation, and 16 % to NIV (CPAP or IPPV).

Discussion

The present study has contributed valuable insights into the effectiveness and possibility of using low-cost equipment to perform HCNC therapy in neonatal care. With a high success rate of 90.9 % in the Neonatal Intensive Care Unit (NICU), regardless of the HFNC-type equipment, has demonstrated its efficacy as a respiratory support method for neonates with ventilatory dysfunction, weaning from NIV and post-extubation therapy.

`There are a number of applications for neonatal HFNC therapy. Clinical situations in which HFNC is being used in neonatology include primary respiratory therapy,[12-14] prematurity apnea,[2] weaning from CPAP,[8-11] and prevention of extubation failure.[4-6] This aligns with the results which showed high extubation success rates with HFNC therapy. Differences in success could be attributed to the different HFNC devices used, but just like the present study, there is no evidence that one equipment is superior to the other.[19] It is possible that previous criteria in the definition of failure may explain, at least in part, the differences in failure rate values. As demonstrated, the post-extubation failure rate at 72 h is lower than at 7 days after extubation.[19] Extending the failure threshold longer carries the risk of including NBs who failed therapy due to unexpected morbidities rather than the underlying respiratory disease. Evidently, extreme prematurity has been identified as a significant risk factor for extubation failure in neonates.[21] Therefore, understanding the role of HFNC in extremely premature infants and optimizing its use in this population requires further investigation.

Weaning from NIV to HFNC has emerged as an important strategy in the management of preterm infants. The present study demonstrated that 66.5 % of the NBs were weaned from NIV to HFNC, with a high success rate of 91.4 %. These findings are consistent with previous studies that have reported successful HFNC weaning from NIV.[8-11] HFNC has been shown to be a safe and effective alternative to NIV in preterm infants, with similar rates of adverse events and no significant difference in the duration of supplemental oxygen or hospital discharge.[8-11] The authors previously demonstrated a 30 % rate of nasal injury resulting from the NIV interface, and this was the main reason for using HFNC for weaning[22]. The reduction in nasal injury and improved patient tolerance of HFNC compared to NIV make it an

attractive option for managing neonates who require continuous positive pressure support.[4,11,15,17,18]

Unlike several previous studies that have focused on HFNC as a primary respiratory support in preterm infants with respiratory distress,[12-14] this study included neonates that were treated with HFNC due to ventilatory dysfunction, with multifactorial causes, including airway disorders and hypoxic-ischemic encephalopathy. These conditions related to structural changes in upper airways or inefficiency of the ventilator muscles could explain the reason for NBs with higher GA have higher HFNC treatment failure.

The evidence base combined with the simple characteristics of the operation of HCFN and its non-invasive nature are attractive for incorporating this therapy in NICUs. It recommended careful clinical indication, adherence to safety standards, adequacy of flow, and FIO2 rates to avoid prolonging therapy and increasing the risk of morbidity.[8-11] The assumption was that HFNC systems did not have distinct effects precisely because the flow generators exhibit similar flow release scales. Obviously, the choice of HFNC varies according to availability and institutional preference. In the meantime, HFNC is becoming widely accepted as a method of non-invasive respiratory support within NICUs the high cost of the commercially available of HFNC equipment can make access difficult in resource-constrained settings. This assumption was confirmed in an economic evaluation of HCFN found that the higher capital equipment costs of CPAP were not outweighed by the higher consumable costs of HFNC.[20,23] In this context, the prospect-adapted obsolete VM could be an interesting alternative for HFNC in NICUs.

While the present study provides valuable insights, it also has limitations. It was not a randomized controlled trial comparing different HFNC equipment, and the sample size was relatively small, especially in the post-extubation group. Therefore, the power to detect differences in failure/success rates between the three types of equipment was limited. The results of this study support the idea that low-cost HFNC therapy is effective for managing respiratory dysfunction, NIV weaning and post-extubation in NICU. Future studies with larger sample sizes and randomization would provide more robust evidence.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

The study received no funding.

Acknowledgments

The authors like to thank the biostatistics unit of the Hospital de Clínicas de Porto Alegre, especially the consultant Vânia Naoni Hirakata.

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