

High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study

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Abstract High-flow nasal cannula (HFNC) is a widely used ventilatory support in children with bronchiolitis in the intensive care setting. No data is available on HFNC use in the general pediatric ward. The aim of this study was to evaluate the feasibility of HFNC oxygen therapy in infants hospitalized in a pediatric ward for moderate–severe bronchiolitis and to assess the changes in ventilatory parameters before and after starting HFNC support. This prospective observational pilot study was carried out during the bronchiolitis season 2011–2012 in a pediatric tertiary care academic center in Italy. Interruptions of HFNC therapy and possible side effects or escalation to other forms of respiratory support were recorded. Oxygen saturation (SpO₂), end-tidal carbon dioxide (ETCO₂), and respiratory rate (RR), measured for a baseline period of 1 h before and at specific time intervals in 48 h after the start of HFNC were recorded. Twenty-seven infants were included (median age 1.3 months; absolute range 0.3–8.5). No adverse events, no premature HFNC therapy termination, and no escalation to other forms of respiratory support were recorded. Median SpO₂ significantly increased by 1–2 points after changing from standard oxygen to HFNC ($p < 0.001$). Median ETCO₂ and RR rapidly decreased by 6–8 mmHg and 13–20 breaths per minute, respectively, in the first 3 h of HFNC therapy ($p < 0.001$) and remained steady thereafter. **Conclusions:** Use of HFNC for oxygen administration is feasible for infants with

moderate–severe bronchiolitis in a general pediatric ward. In these children, HFNC therapy improves oxygen saturation levels and seems to be associated with a decrease in both ETCO₂ and RR.

Keywords Bronchiolitis · Oxygen inhalation therapy · Children · Carbon dioxide

Abbreviations

ETCO ₂	End-tidal carbon dioxide
FiO ₂	Fraction of inspired oxygen
HFNC	High-flow nasal cannula
HR	Heart rate
PICU	Pediatric intensive care unit
RR	Respiratory rate
RSV	Respiratory syncytial virus
SpO ₂	Oxygen saturation

Introduction

Bronchiolitis is the most common lower respiratory tract infection in the first year of life and the leading cause of hospitalization in infants [3, 33]. Despite the growing literature investigating treatment options with recent positive data about the use of nebulized hypertonic saline and epinephrine [11, 32], oxygen supplementation still remains the mainstay of therapy [19].

Oxygen therapy administered by heated, humidified high-flow nasal cannulae (HFNC) has been shown to reduce the intubation rate and to improve respiratory distress in children hospitalized in intensive care units for bronchiolitis [19, 22]. HFNC has proven to be a well tolerated, non-invasive respiratory support which provides a humidified and heated air-oxygen blend at a flow of 1 to 8 l/min [19, 22]. HFNC are thought to improve the ventilatory status by prevention of

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mucous dryness and improvement of mucous-ciliary clearance, reduction of energy expenditure for gas warming and humidification, and provision of continuous positive airway pressure, which contributes to the maintenance of patent alveoli, improves the ventilation–perfusion mismatch, and prevents microatelectasis [6, 9, 12].

The advantages of HFNC over nasal continuous positive airways pressure, i.e., its ease of use and improved tolerance with minimal nasal trauma, have led to increasing utilization also outside the intensive care unit [10, 17, 30]. However, there is a current lack of data on the feasibility of HFNC in infants with bronchiolitis managed on the pediatric ward and its effects on ventilation status have not been thoroughly investigated. HFNC oxygen therapy has been introduced as a standard of care at our institution for use in patients with bronchiolitis admitted to the general pediatric ward since September 2011. This decision was based on local expert consensus. The aim of this study was to evaluate the feasibility of oxygen therapy administered via HFNC in infants hospitalized for moderate–severe bronchiolitis in a regular pediatric ward and to assess the changes in ventilatory parameters before and after starting HFNC support.

Methods

Study design and setting

A prospective observational pilot study of admitted infants with moderate–severe bronchiolitis who received HFNC oxygen therapy on a pediatric ward at the University of Padova Hospital (Italy), from November 2011 to April 2012. Our Pediatric Department is provided with a pediatric intensive care unit (PICU) and a rapid admission process for deteriorating in-patients. Education on HFNC use was provided to medical and nursing staff working in the general pediatric ward by means of a dedicated half-day course, including lectures and practice (i.e., hands-on session on how to assemble the HFNC device and disposable materials, how to provide good equipment maintenance, and to monitor good functioning). After the course, a dedicated procedure on HFNC use was also available in the quality system of the hospital intranet (IO-PED2-007). A trained member of the respiratory team was readily available in case of any problem related to HFNC use.

Definitions

Bronchiolitis was defined as the first viral episode of respiratory distress, accompanied by coryza, cough, crepitations, and/or wheezing [23]. Day of disease was counted from date of onset of respiratory symptoms (rhinorrhea, cough, respiratory distress) as reported by parents.

Inclusion and exclusion criteria

Neonates and infants aged 7 days to 12 months who were hospitalized for their first episode of moderate–severe bronchiolitis and required oxygen therapy were enrolled in the study. Exclusion criteria included recurrent wheezing, underlying hemodynamically significant heart disease, chronic lung disease, neuromuscular disease, oxygen therapy at home, and tracheostomy.

Clinical evaluation and management

Bronchiolitis severity was assessed according to our emergency department bronchiolitis protocol using a score adapted from Wang et al. [28] (see [Appendix](#)). Moderate bronchiolitis was defined by a score of >5 and severe by a score of >10 . According to the protocol, children with moderate and severe bronchiolitis received oxygen therapy with nebulized 3 % hypertonic saline when presenting an oxygen saturation (SpO₂) ≤ 92 %, i.e., with 2 or 3 points on the item “oxygen saturation” of the severity score (see [Appendix](#)). Only children with moderate–severe bronchiolitis needing oxygen supplementation according to the emergency department protocol were included in the study.

Hypertonic saline was introduced as a standard of care in our emergency department since 2010 for patients with moderate–severe bronchiolitis who needed oxygen supplementation, based on local expert consensus and available evidence [18]. A trial of nebulized salbutamol was given if audible wheezing was present. Children with severe bronchiolitis received oxygen therapy and nebulized epinephrine 0.25 mg/kg in 3 % hypertonic saline. In the emergency department, standard oxygen therapy, up to 2 l/min through regular nasal cannula, was administered. HFNC oxygen therapy was started once infants were admitted to the ward.

Feasibility evaluation

Unanticipated interruptions of HFNC oxygen therapy due to difficulties in management of the device or patient intolerance to nasal cannulae, as reported either by nurses or medical staff, were recorded. Side effects to HFNC use, such as nasal mucosa trauma and/or bleeding, vomiting (as a possible result of gastric distension), and pneumothorax, as well as the need for escalation to other forms of respiratory support, were monitored and recorded. All this data was collected in a dedicated checklist form that was reviewed during the daily ward rounds and was then entered into the electronic database along with patients’ data that were collected in the clinical report form.

Vital signs recording

Oxygen saturation, respiratory rate (RR), heart rate (HR), body temperature, and end-tidal carbon dioxide (ETCO₂)

were recorded for each patient for a baseline period of 1 h (t-1 and t0) before HFNC positioning. Oxygen saturation at baseline (t-1 and t0) was recorded with standard oxygen and at room air. The same parameters were then recorded at 1 h (t1), 3 h (t3), 6 h (t6), 12 h (t12), 24 h (t24), 36 h (t36), and 48 h (t48) after the start of HFNC. A nasopharyngeal aspirate for viral detection through real time PCR was performed in all infants. Additional tests were undertaken according to the treating physician.

Instrumentation and devices

Vital signs monitor

SpO₂ and HR were recorded using the Monitor Agilent M3046A-Philips; RR was manually measured counting the breaths per minute.

ETCO₂

End-tidal CO₂ was monitored using nasal cannulae (Philips CapnoLine H Infant/Neonatal) specific for infants less than 10 kg [5] and connected to the Monitor Agilent M3046A-Philips. Nasal cannulae for oxygen administration were removed for the time required for the ETCO₂ measurement. Capnography was monitored for 1 min, during which, time values were recorded every 10 s. The final ETCO₂ values used for data analysis were the mean of all six recordings (every 10 s for a minute).

HFNC

The Fisher & Paykel Healthcare heated humidified HFNC system (MR850 humidification system, RT329 Kit and Optiflow oxygen cannulas; Fisher & Paykel Healthcare, Auckland, New Zealand) was used in all patients. The low-resistance nasal cannulas (Fisher and Paykel Healthcare) included an intermediate cannula BC 2755 base diameter 3.4±0.77 mm, tip diameter 2.7±0.56 mm, with a maximum flow rate of 7 l/min and a pediatric cannula BC 7380 base diameter 4.6±0.7 mm, tip diameter 4.25±0.75 mm, with a maximum flow rate of 8 l/min. The size of the cannulas fitted the child's nares without occlusion. The flow rate was determined using a derived formula [27]: flow rate (in liters per minute) = weight (in kilograms)+1, with a maximum flow rate of 8 l/min and a constant flow temperature of 37 °C. This choice was made in order to deliver a flow greater than the patient minute ventilation, so that effective fraction of inspired oxygen (FiO₂) equals the nasal cannula oxygen concentration by preventing mixing with room air, and to minimize possible adverse events related to delivery of inadvertently too high positive end expiratory pressure for the patient. The system has an integrated pressure relief valve

(manifold) at its input port to limit the maximum system pressure. This valve is set at 45-cm H₂O.

The inspired oxygen concentration was adjusted to achieve a SpO₂ ≥94 %. Flow rate was weaned by 1 l/min every 6 h when adequate oxygen saturations were maintained with a FiO₂ of 25 %. HFNC was stopped and switched to standard oxygen therapy, if necessary, once the patients remained stable with a flow of 2 l/min.

Statistical analysis

Continuous variables were expressed as medians and absolute ranges. The overall comparison of repeated measures over time was carried out by means of Friedman test (two-way analysis of variance by ranks). Comparisons between each measure at baseline (t-1 and t0) and each time point after initiation of HFNC were then carried out by means of Wilcoxon test for paired samples. Categorical variables were expressed as numbers and percentages. Parameters displaying $p < 0.05$ were considered statistically significant. Statistical analyses were conducted using the statistical program MedCalc 11.1.

The study was reviewed and approved by the Hospital Ethics Committee, approval number 2476P, and informed consent was obtained from the parents or legal guardians.

Results

Of the 80 infants less than 1 year of age hospitalized for bronchiolitis during the study period, 42 were not eligible because of mild bronchiolitis (clinical score ≤5). Thirty-eight patients presented a moderate–severe bronchiolitis and 27 were finally enrolled (Fig. 1).

Demographic and clinical characteristics of study patients are reported in Table 1. Twenty-two patients were under 3 months of age. Nineteen patients were hospitalized between December and January.

There were no cases of unanticipated interruptions of HFNC oxygen administration and the therapy was well tolerated by all study patients with no need for sedation. There were no cases of pneumothorax or any other reported adverse events. None of the study patients were admitted to the intensive care unit because of the need of escalation to other forms of respiratory support.

After changing from standard oxygen to HFNC, SpO₂ showed a statistically significant increase—Table 2. Median FiO₂ administered to achieve target saturation was 40 % (as set in the device) in the first 12 h and slightly reduced thereafter—Table 2. The comparison between repeated measurements of ETCO₂ and RR over time resulted significantly different as per Friedman test ($p < 0.001$). Median ETCO₂ and RR decreased after initiation of HFNC at all time

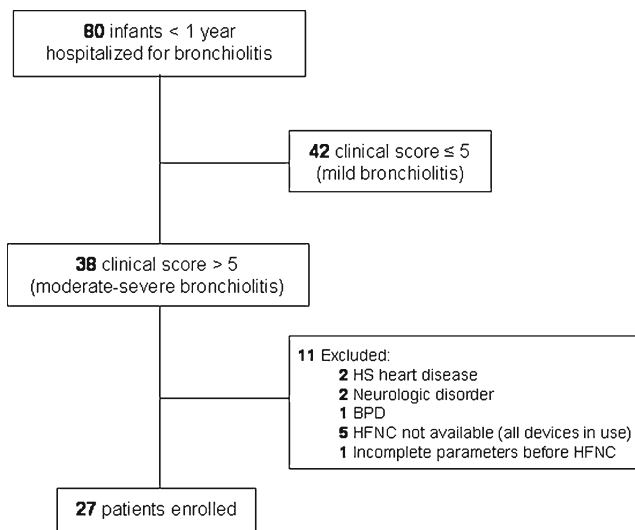


Fig. 1 Patients flow-chart. *HFNC* high-flow nasal cannulae; *HS* hemodynamically significant; *BPD* bronchopulmonary dysplasia

intervals ($p < 0.001$ for each comparison between the baseline period (t-1, t0) and during HFNC therapy, (t1–t48))—Table 2, Figs. 2 and 3. No difference was observed in the time course of HR values.

Discussion

In this pilot study, we describe the use of oxygen therapy delivered via HFNC in infants hospitalized for moderate-severe bronchiolitis in a pediatric ward and its effects on ventilatory parameters. Our results show that HFNC oxygen therapy is a feasible delivery system for oxygen administration in a pediatric ward. It provides optimal oxygen saturation levels and is associated with a decrease in both ETCO_2 and RR.

Effective non-invasive respiratory support in children with moderate-severe bronchiolitis is important in order to improve comfort by reducing work of breathing, and to prevent complications such as atelectasis as well as progressive respiratory exhaustion which may lead to respiratory failure. HFNC respiratory support has been well-tolerated with few adverse effects in both children [13, 19, 22] and pre-term neonates [6] in pediatric and neonatal intensive care units. In pre-term infants, HFNC have mainly been evaluated for the treatment of apnea of prematurity [25], respiratory distress syndrome, and the prevention of extubation failure [4, 15, 24, 31]. However, its effectiveness compared to traditional nasal-CPAP has not been rigorously studied [6, 7, 29].

The increasing availability of HFNC devices in the intensive care setting over the past few years, as well as its tolerance and ease of use, has prompted use in other respiratory diseases such as bronchiolitis. The first studies assessing

the usefulness of HFNC in children with bronchiolitis were carried out in PICU in the United States and Australia [19, 22]. McKiernan et al. [19] retrospectively studied 115 children (57 from before the introduction of HFNC and 58 from the season after the introduction of HFNC) and showed a 68 % decrease in intubations and a decrease in the median PICU length of stay from 6 to 4 days after the introduction of HFNC. Australian investigators noted a decline in intubation rate from 37 to 7 %, with no adverse events, in a retrospective chart review over a 5-year period of 167 children with bronchiolitis treated with HFNC in the PICU [21]. Similar to our results, both studies found a reduction in respiratory rate at 60 [19] and 90 min [22] after initiation of HFNC therapy.

A randomized controlled trial [14] of 19 infants with bronchiolitis showed a higher median SpO_2 in patients

Table 1 Clinical and demographic characteristics of study patients

Variable	Results
Age in months (median, range)	1.3 (0.3–8.5)
Age <6 months (<i>n</i>)	24
History of Prematurity	
32–36 wg (<i>n</i>)	4
28–32 wg (<i>n</i>)	2
Sex (female/male)	13/14
Weight in Kg (median, range)	4.2 (2.6–7.2)
Day of illness at hospitalization (median, range)	2 (1–8)
Clinical Score at t0 (<i>n</i>)	
6–10	23
>10	4
Viral status (<i>n</i>)	
RSV	14
RSV—Rhinovirus	7
RSV—Coronavirus	1
RSV—Rhinovirus—Coronavirus	1
Adenovirus—Bocavirus—Rhinovirus	2
Unknown	2
Chest x-rays performed (<i>n</i>)	22
Major abnormality on chest x-rays (<i>n</i>)	3*
Nebulized therapy prior to HFNC	
3 % hypertonic saline (<i>n</i>)	27
Salbutamol (<i>n</i>)	20
Epinephrine (<i>n</i>)	4
Intravenous fluid replacement therapy (≥ 24 h) (<i>n</i>)	25
Duration of HFNC (days) (median, range)	5 (3–14)
Length of hospitalization (days) (median, range)	8 (4–15)

Range absolute range, *wg* week gestation, *HFNC* high-flow nasal cannulae, *t0* immediately before HFNC positioning, *RSV* respiratory syncytial virus

*1 lobar atelectasis and 2 lobar consolidations. Major abnormalities on the chest x-rays for the purpose of this study were defined as: lobar atelectasis, lobar consolidations, or pneumothorax

Table 2 Parameters variation over time, at baseline (t-1 and t0) and during HFNC therapy (t1–t48)

Parameters	t-1	t0	t1	t3	t6	t12	t24	t36	t48
ETCO ₂ , mmHg	36 (27–50)	37 (27–50)	30 (20–41)	29 (20–42)	30 (17–50)	30 (19–42)	29 (19–41)	29 (15–42)	29 (18–36)
RR, breaths per minute	67 (35–90)	70 (40–88)	50 (30–80)	54 (38–75)	50 (30–70)	47 (27–80)	50 (30–80)	42 (25–60)	45 (30–60)
HR, beats per minute	147 (120–170)	150 (130–170)	140 (120–175)	145 (123–176)	150(111–195)	146 (121–187)	148 (113–173)	141 (105–172)	140 (108–180)
Sat O ₂ , %	89 (82–93)¶/96 (90–99)§	88±(85–91)/97 (91–100)§	97 (93–100)	98 (94–100)	98 (94–100)	99 (95–100)	98 (94–100)	99 (94–100)±2	98 (93–100)
FiO ₂ , %	21/n.c.	21/n.c.	40 (25–100)	40 (25–100)	40 (25–100)	40 (25–100)	37 (30–90)	37 (25–90)	35 (21–90)
Fever >37.5 °C (n)	2	0	1	2	3	2	1	0	2

Paired comparisons were performed between values at t-1 and t0 with values at each time point after the start of HFNC (t1–t48). Data are reported as medians and absolute ranges. ETCO₂; $p \leq 0.001$ for each comparison; RR $p \leq 0.001$ for each comparison; SpO₂ $p < 0.001$ for each comparison between values recorded during regular nasal cannulae delivered oxygen at baseline (§) and during HFNC; RR respiratory rate; HR heart rate; SpO₂ oxygen saturation; FiO₂ fraction of inspired oxygen; HFNC high-flow nasal cannulae; NS not significant; n.c. regular nasal cannulae delivered oxygen

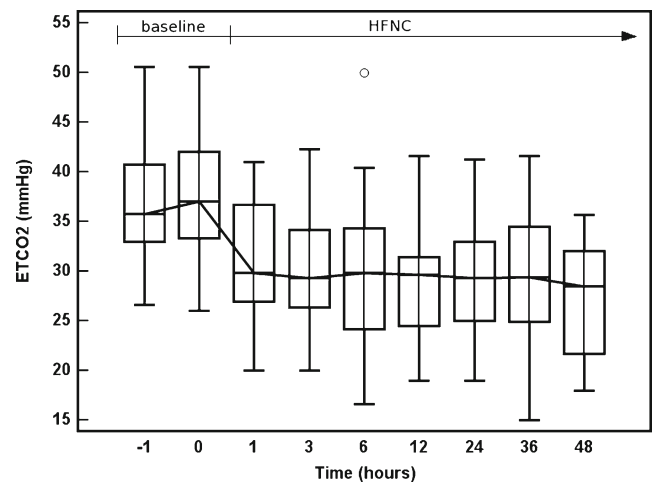


Fig. 2 ETCO₂ values distribution over time pre- (*baseline*) and during HFNC therapy. The box-whisker plots show the median (*horizontal line*), the interquartile range (*margins of box*), the absolute range (*vertical line*) and outlier values (*circle*). ETCO₂ end-tidal CO₂; HFNC high-flow nasal cannulae

receiving HFNC oxygen therapy compared with head-box oxygen at 8 h (100 vs. 96 %, $p=0.04$) and 12 h (99 vs. 96 %, $p=0.04$). Total time in oxygen, time to feed, time to discharge, and total length of stay, were similar between groups. As acknowledged by the authors, the study was limited by the small sample size, the non-blinded intervention, and the lack of any formal measure of pulmonary mechanics or gas exchange other than SpO₂. While the same authors express concern about the possibility that HFNC therapy with high concentrations of oxygen may provide falsely, reassuring oxygenation in sick infants who are, in fact, tiring, our study shows that HFNC offers some ventilatory support as well, as reflected by the steady decrease in ETCO₂ and RR after

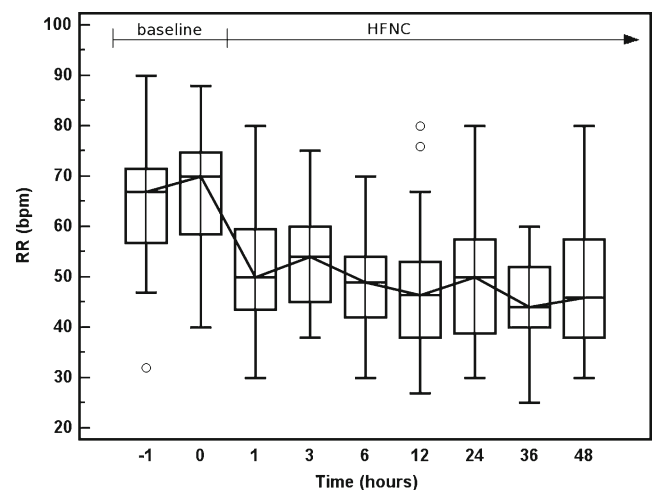


Fig. 3 RR values distribution over time pre- (*baseline*) and during HFNC therapy. The box-whisker plots show the median (*horizontal line*), the interquartile range (*margins of box*), the absolute range (*vertical line*) and outlier values (*circles*). RR respiratory rate in breaths per minute (bpm); HFNC high-flow nasal cannulae

initiation of HFNC oxygen delivery. None of our children needed escalation to other forms of respiratory support suggesting that the decrease in ETCO_2 and RR may identify responders to therapy. In the study by Shibley et al. [22], responders to HFNC showed a 20 % decrease in RR within 90 min of the start of HFNC therapy, whereas non-responders showed little change in RR. ETCO_2 , however, was not measured.

A more recent study carried out in PICU has shown a decrease in RR in infants with bronchiolitis who responded to HFNC therapy, compared with the nonresponder group [1]. The same authors reported a decrease in PCO_2 on blood gas analysis, with significantly higher initial PCO_2 values in the nonresponder patients [1].

Measurement of ETCO_2 with capnography is a non-invasive indirect measurement of blood CO_2 tension with fast response time to changes in blood levels. It allows for visual inspection of changes in CO_2 concentrations by means of a waveform display. The principal determinants of ETCO_2 are alveolar ventilation, pulmonary perfusion (cardiac output), and metabolic status [16]. The present study is the first to evaluate the effect of HFNC therapy on gas exchange by means of ETCO_2 measurement in patients with bronchiolitis. Despite arterial blood gas analysis being the gold standard of monitoring partial pressure of arterial carbon dioxide, this is an invasive procedure and it is rarely useful at admission (or later if there is clinical improvement) for patients with bronchiolitis. It can increase stress and work of breathing of these acutely ill infants, which may in turn, worsen their respiratory status. ETCO_2 has shown good correlation with capillary and arterial CO_2 in both adults and children [2, 21, 26] and is especially useful for detecting trends in ventilatory status.

This study has several limitations. First, it is not a randomized controlled trial, so differences with standard oxygen therapy cannot be evaluated and compared in terms of effects on ventilation status, length of stay, or effectiveness in preventing the need for further ventilatory support. The lack of a comparison group does not allow for control of confounding factors and it may be argued that other interventions (nasal suction, use of hypertonic saline, salbutamol/adrenaline) during ED stay might have influenced our findings. However, if this had been the case, improvement of ETCO_2 and RR would have been expected between $t-1$ and t_0 , when children received the above mentioned interventions, as opposed to the steady ETCO_2 and RR values found at these times in our study. Nevertheless, even if a significant decrease in these parameters was recorded only after HFNC start, a delayed contribution of other interventions cannot be completely excluded.

Compared to other study cohorts [14, 19, 22] our sample size mainly includes young infants under 3 months of age, who are most commonly at higher risk of moderate–severe

disease because of the narrower respiratory airways, reduced respiratory reserve, and higher metabolic demands. This peculiar feature may explain the longer length of stay in our study, while no data on HFNC influence on length of stay can be drawn from our study design. A recent Spanish study [10] assessing the effects of HFNC in a similar cohort of very young patients on the ward, reported similar results in terms of duration of oxygen therapy (median of 4 days) and length of hospitalization (median of 9 days).

Finally, the small sample size of our study should be noted. However, it was designed as a pilot study and our results may provide useful data for future well-designed randomized controlled trials.

The possibility to manage infants with bronchiolitis outside the PICU has important economic implications as pediatric critical care is expensive and sometimes difficult to access. In contrast to nasal-CPAP which is often poorly tolerated and is impractical outside the intensive care setting [7, 8], HFNC provides a well-tolerated, easy to use and safe respiratory support, that should be considered for infants with moderate–severe bronchiolitis needing oxygen supplementation, hospitalized in a pediatric ward. Despite the fact that our small sample size does not allow to properly assess the safety of this intervention on the ward, possible harm related to HFNC is rare according to the published literature. So far, only one report of a significant pneumothorax requiring intubation has been reported in a 2-month-old child who was receiving HFNC at a flow of 8 l/min for bronchiolitis [13].

However, our results cannot support that HFNC can be safely introduced widely on a general pediatric ward even in centers not provided with an intensive care unit facility. In these settings, careful medical judgment based on patient's clinical status and knowledge of the system network and pathways for deteriorating patients should always drive clinical decision making in the first place. Randomized controlled studies are needed to confirm the findings of this pilot study and to assess HFNC effect on other outcomes, such as improved enteral feeding, reduction in transfer to the intensive care unit, intubation rate, and length of hospitalization, as well as long-term benefits and economic impact for the healthcare system.

Conclusion

Use of HFNC for oxygen administration is feasible for infants with moderate–severe bronchiolitis who are hospitalized in the ward and need supplemental oxygen. HFNC therapy improves oxygen saturation levels and seems to be associated with a decrease in both ETCO_2 and RR.

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Conflict of interest Dr. Krauss is a consultant for Oridion Medical, a capnography company, and holds three patents in the area of capnography. The other authors have no conflicts of interest or funding to disclose. The authors have not received any financial support, salary, or other personal benefits by Fisher & Paykel Healthcare for the present study and do not hold stock in the company.

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Appendix

Bronchiolitis severity score (modified by Wang et al. [28])

Illness severity	Score
Mild	≤5
Moderate	6–10
Severe	>10

	Clinical assessment	Points
General appearance	Quiet, sleeping	0
	Crying when touched, but easy to console	1
	Moderately irritable, difficult to console	2
	Extremely irritable, lethargic, poor feeding	3
Chest sounds	No crepitations, no wheezing	0
	Diffuse crepitations or terminal expiratory wheezing	1
	Entire expiration wheezing	2
	Diffuse inspiratory and expiratory wheezing	3
Dyspnea	None	0
	Mild (intercostal retractions)	1
	Moderate (tracheo-sternal retractions)	2
	Severe (severe retractions with nasal flaring)	3
Respiratory rate	<40 bpm	0
	40–55 bpm	1
	56–65 bpm	2
	>65 bpm	3
	Oxygen saturation	>96 %
	93–95 %	1
	90–92 %	2
	<90 %	3

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