



Literature list
**High flow O₂ therapy with
high flow nasal canula (HFNC)**
for neonates and paediatric patients

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Authors	Subject	Publication
Wilkinson D et al.	High flow nasal cannula for respiratory support in preterm infants	<u>Cochrane Library</u>

Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD006405

Abstract

Background

High flow nasal cannulae (HFNC) are small, thin, tapered binasal tubes that deliver oxygen or blended oxygen/air at gas flows of more than 1 L/min. HFNC are increasingly being used as a form of non-invasive respiratory support for preterm infants.

Objectives

To compare the safety and efficacy of HFNC with other forms of non-invasive respiratory support in preterm infants.

Conclusion

HFNC has similar rates of efficacy to other forms of non-invasive respiratory support in preterm infants for preventing treatment failure, death, and CLD.

Most evidence is available for the use of HFNC as post-extubation support. Following extubation, HFNC is associated with less nasal trauma, and may be associated with reduced pneumothorax compared with nasal CPAP.

Further adequately powered randomised controlled trials should be undertaken in preterm infants comparing HFNC with other forms of primary non-invasive support after birth and for weaning from non-invasive support. Further evidence is also required for evaluating the safety and efficacy of HFNC in extremely preterm and mildly preterm subgroups, and for comparing different HFNC devices.

Authors	Subject	Publication
Roberts CT, Hodgson KA	Nasal high flow treatment in preterm infants	Maternal Health, Neonatology and Perinatology

Maternal Health, Neonatology and Perinatology volume 3, Article number: 15 (2017)

Abstract

Nasal High Flow (HF) is a mode of 'non-invasive' respiratory support for preterm infants, with several potential modes of action, including generation of distending airway pressure, washout of the nasopharyngeal dead space, reduction of work of breathing, and heating and humidification of inspired gas. HF has several potential advantages over continuous positive airway pressure (CPAP), the most commonly applied form of non-invasive support, such as reduced nasal trauma, ease of use, and infant comfort, which has led to its rapid adoption into neonatal care. In recent years, HF has become a well-established and commonly applied treatment in neonatal care.

Recent trials comparing HF and CPAP as primary support have had differing results. Meta-analyses suggest that primary HF results in an increased risk of treatment failure, but that 'rescue' CPAP use in those infants with HF failure results in no greater risk of mechanical ventilation. Even in studies with higher rates of HF failure, the majority of infants were successfully treated with HF, and rates of important neonatal morbidities did not differ between treatment groups. Importantly, these studies have included only infants born at ≥ 28 weeks' gestational age (GA). The decision whether to apply primary HF will depend on the value placed on its advantages over CPAP by clinicians, the approach to surfactant treatment, and the severity of respiratory disease in the relevant population of preterm infants.

Post-extubation HF use results in similar rates of treatment failure, mechanical ventilation, and adverse events compared to CPAP. Post-extubation HF appears most suited to infants ≥ 28 weeks; there are few published data for infants below this gestation, and available evidence suggests that these infants are at high risk of HF failure, although rates of intubation and other morbidities are similar to those seen with CPAP. There is no evidence that using HF to 'wean' off CPAP allows for respiratory support to be ceased more quickly, but given its advantages it would appear to be a suitable alternative in infants who require ongoing non-invasive support. Safety data from randomised trials are reassuring, although more evidence in extremely preterm infants (< 28 weeks' GA) is required.

Conclusion

High Flow is now well established as an important part of neonatal respiratory care and has a number of potential benefits for preterm infants. While it appears that HF can be applied successfully as primary support for many infants > 28 weeks' GA, it is less effective than CPAP in preventing treatment failure, and factors such as severity of RDS in the treated population, and approach to surfactant should be considered. The evidence suggests that post-extubation HF is suitable for infants > 28 weeks' GA. The availability of rescue CPAP is an important part of the treatment pathway in both primary and post-extubation use, ensuring infants treated with HF are not at increased risk of intubation. Research into the optimal approach to weaning HF, and its use in extremely preterm infants, is required to ensure it is applied in such a way that produces maximal benefit for infants and their families, whilst avoiding unintended adverse effects.

Authors	Subject	Publication
Haut C	Pediatric Noninvasive Ventilation	PubMed

J Pediatr Intensive Care. 2015 Jun;4(2):121-127. doi: 10.1055/s-0035-1556754.

Abstract

Noninvasive ventilation has been available for many years for use in the pediatric population. Historically, continuous positive airway pressure and bilevel positive airway pressure modes were used for respiratory diseases, including neonatal apnea, bronchiolitis, asthma, and pneumonia. Newer studies suggest that noninvasive ventilation is also an effective and safe mode for support of children with acute respiratory distress syndrome and respiratory failure. The newest type of noninvasive respiratory support is high flow nasal cannula, which has gained popularity in the past few years and its use is being justified in the literature. Studies have shown that these therapies can decrease the need for intubation and ventilation, decrease length of intensive care days, and increase patient comfort. Additional research is needed to support optimal setting selection and recommendations for the use of noninvasive therapies for infants and children.

Summary

NIV in the form of CPAP, BiPAP, or HFNC can be an effective, safe, and financially responsible mode of providing respiratory support in a variety of pediatric conditions as compared with intubation and mechanical ventilation. Care of the child receiving therapy requires monitoring for complications or side effects and measuring efficacy. Determining when increased support is necessary is extremely important in the management plan. Further research studies in the form of randomized controlled trials are needed to document which mode provides the best support with the highest level of safety.

Authors	Subject	Publication
Yoder BA et al.	Heated, humidified high-flow nasal cannula versus nasal CPAP for respiratory support in neonates	PubMed

Randomized Controlled Trial Pediatrics. 2013 May;131(5):e1482-90. doi: 10.1542/peds.2012-2742. Epub 2013 Apr 22.

Abstract

Background and objective

Heated, humidified high-flow nasal cannula (HHHFNC) is commonly used as a noninvasive mode of respiratory support in the NICU. The safety and efficacy of HHHFNC have not been compared with other modes of noninvasive support in large, randomized trials. The objective was to assess the efficacy and safety of HHHFNC compared with nasal continuous positive airway pressure (nCPAP) for noninvasive respiratory support in the NICU.

Methods

andomized, controlled, unblinded noncrossover trial in 432 infants ranging from 28 to 42 weeks' gestational age with planned nCPAP support, as either primary therapy or postextubation. The primary outcome was defined as a need for intubation within 72 hours of applied noninvasive therapy.

Results

There was no difference in early failure for HHHFNC (23/212 [10.8%]) versus nCPAP (18/220 [8.2%]; $P = .344$), subsequent need for any intubation (32/212 [15.1%] vs 25/220 [11.4%]; $P = .252$), or in any of several adverse outcomes analyzed, including air leak. HHHFNC infants remained on the study mode significantly longer than nCPAP infants (median: 4 vs 2 days, respectively; $P < .01$), but there were no differences between study groups for days on supplemental oxygen (median: 10 vs 8 days), bronchopulmonary dysplasia (20% vs 16%), or discharge from the hospital on oxygen (19% vs 18%).

Conclusions

Among infants ≥ 28 weeks' gestational age, HHHFNC appears to have similar efficacy and safety to nCPAP when applied immediately postextubation or early as initial noninvasive support for respiratory dysfunction.

Authors	Subject	Publication
Lee JH et al.	Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature	PubMed

Review Intensive Care Med. 2013 Feb;39(2):247-57. doi: 10.1007/s00134-012-2743-5. Epub 2012 Nov 10.

Abstract

Background

High flow nasal cannula (HFNC) systems utilize higher gas flow rates than standard nasal cannulae. The use of HFNC as a respiratory support modality is increasing in the infant, pediatric, and adult populations as an alternative to non-invasive positive pressure ventilation.

Objectives

This critical review aims to: (1) appraise available evidence with regard to the utility of HFNC in neonatal, pediatric, and adult patients; (2) review the physiology of HFNC; (3) describe available HFNC systems (online supplement); and (4) review ongoing and planned trials studying the utility of HFNC in various clinical settings.

Results

Clinical neonatal studies are limited to premature infants. Only a few pediatric studies have examined the use of HFNC, with most focusing on this modality for viral bronchiolitis. In critically ill adults, most studies have focused on acute respiratory parameters and short-term physiologic outcomes with limited investigations focusing on clinical outcomes such as duration of therapy and need for escalation of ventilatory support. Current evidence demonstrates that HFNC generates positive airway pressure in most circumstances; however, the predominant mechanism of action in relieving respiratory distress is not well established.

Conclusion

Current evidence suggests that HFNC is well tolerated and may be feasible in a subset of patients who require ventilatory support with non-invasive ventilation. However, HFNC has not been demonstrated to be equivalent or superior to non-invasive positive pressure ventilation, and further studies are needed to identify clinical indications for HFNC in patients with moderate to severe respiratory distress.

Authors	Subject	Publication
Osman M et al.	Assessment of pain during application of nasal-continuous positive airway pressure and heated, humidified high-flow nasal cannulae in preterm infants	Journal of Perinatology

Nature > journal of perinatology > original article > Published: 27 November 2014

Abstract

Objective

To assess pain and compare its severity in preterm infants during application of nasal-continuous positive airway pressure (nCPAP) and heated, humidified high-flow nasal cannulae (HHHFNC).

Study Design

An observational cross-sectional study. Sixty preterm infants, categorized into nCPAP (n=37) and HHHFNC groups (n=23). Pain response was assessed using Premature Infant Pain Profile (PIPP), duration of first cry and salivary-cortisol concentrations.

Result

The PIPP scores were significantly higher in the nCPAP compared with HHHFNC group (10 (7–12) vs 4 (2–6), $P<0.01$). None of the infants in the HHHFNC group had severe pain defined as a PIPP score >12 , compared with 5 (13.5%) infants in the nCPAP group. Salivary-cortisol concentrations were significantly higher in nCPAP group compared with the HHHFNC group (5.0 (3.6–5.9) vs 1.6 (1.0–2.3) nmol l⁻¹, $P<0.01$). A lower incidence of cry was observed for infants in the HHHFNC group compared with the nCPAP group (11 (47.8%) vs 30 (81.1%), $P<0.001$), however, the duration of first cry was not significantly different between groups. The respiratory rate was significantly lower after application of HHHFNC compared with nCPAP ($P<0.001$). There were no significant differences between groups with regard to fraction of inspired oxygen (FiO₂), oxygen saturation by pulse oximeter (SpO₂) and heart rate.

Conclusion

The application of HHHFNC in preterm infants is associated with less pain compared with nCPAP, as it is associated with less PIPP scores and lower salivary-cortisol concentrations.

Authors	Subject	Publication
Klingenberg C et al.	Patient comfort during treatment with heated humidified high flow nasal cannulae versus nasal continuous positive airway pressure: a randomised cross-over trial	PubMed

Randomized Controlled Trial Arch Dis Child Fetal Neonatal Ed. 2014 Mar;99(2):F134-7.
doi: 10.1136/archdischild-2013-304525. Epub 2013 Nov 13.

Abstract

Objective

To compare patient comfort in preterm infants treated with heated humidified high flow nasal cannulae (HHHFNC) versus nasal continuous positive airway pressure (NCPAP).

Design

Randomised cross-over trial (2×24 h).

Setting

Single tertiary neonatal unit.

Patients

20 infants less than 34 weeks postmenstrual age treated with NCPAP due to mild respiratory illness.

Main outcome measures

Primary outcome was patient comfort assessed by the EDIN (neonatal pain and discomfort) scale. Secondary outcomes were respiratory parameters (respiratory rate, FiO₂, SpO₂, TcPCO₂), ambient noise, salivary cortisol and parental assessments of their child.

Results

We found no differences between HHHFNC and NCPAP in mean cumulative EDIN score (10.7 vs 11.1, p=0.25) or ambient noise (70 vs 74 dBa, p=0.18). Parents assessed HHHFNC treatment as significantly better in the three domains, 1) child satisfied, 2) parental contact and interaction and 3) possibility to take part in care. Mean respiratory rate over 24 h was lower during HHHFNC than CPAP (41 vs 46, p=0.001). Other respiratory parameters were similar.

Conclusions

Using EDIN scale, we found no difference in patient comfort with HHHFNC versus NCPAP. However, parents preferred HHHFNC, and during HHHFNC respiratory rate was lower than during NCPAP.

Authors	Subject	Publication
Shatty S et al.	Work of breathing during CPAP and heated humidified high-flow nasal cannula	PubMed

Randomized Controlled Trial Arch Dis Child Fetal Neonatal Ed. 2016 Sep;101(5):F404-7.
doi: 10.1136/archdischild-2015-309310. Epub 2016 Jan 14.

Abstract

Objective

To determine whether continuous positive airway pressure (CPAP) compared with heated humidified, high-flow nasal cannula (HHFNC) in infants with evolving or established bronchopulmonary dysplasia (BPD) reduced the work of breathing (WOB) and thoracoabdominal asynchrony (TAA) and improved oxygen saturation (SaO₂).

Design

Randomised crossover study.

Setting

Tertiary neonatal unit.

Patients

20 infants (median gestational age of 27.6 weeks (range 24.6-31.9 weeks)) were studied at a median postnatal age of 30.9 weeks (range 28.1-39.1 weeks).

Interventions

Infants were studied on 2 consecutive days. On the first study day, they were randomised to either CPAP or HHFNC each for 2 h, the order being reversed on the second day.

Main outcome measures

The WOB was assessed by measuring the pressure time product of the diaphragm (PTPdi). PTPdi, TAA and SaO₂ were assessed during the final 5 min of each 2 h period and the results on the two study days were meaned.

Results

There were no significant differences in the results on CPAP versus HHFNC: mean PTPdi 226 (range 126-294) versus 224 cm H₂O/s/min (95% CI for difference: -27 to 22; p=0.85) (range 170-318) (p=0.82), mean TAA 13.4° (range 4.51°-23.32°) versus 14.01° (range 4.25°-23.86°) (95% CI for difference: -3.9 to 2.8; p=0.73) (p=0.63) and mean SaO₂ 95% (range 93%-100%) versus 95% (94%-99%), (95% CI for difference -1.8 to 0.5; p=0.25) (p=0.45).

Conclusion

In infants with evolving or established BPD, CPAP compared with HHFNC offered no significant advantage with regard to the WOB, degree of asynchrony or oxygen saturation.

Authors	Subject	Publication
Saslow JG et al.	Work of breathing using high-flow nasal cannula in preterm infants	PubMed

Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD00Randomized Controlled Trial J Perinatol. 2006 Aug;26(8):476-80. doi: 10.1038/sj.jp.7211530. Epub 2006 May 11.6405

Abstract

Objective

To compare the work of breathing (WOB) in premature neonates supported with high-flow nasal cannula (HFNC) and nasal continuous positive airway pressure (NCPAP).

Study design

Eighteen preterm neonates <2.0 kg on HFNC or NCPAP support were studied in a random order. A ventilator was used to deliver 6 cm H₂O of NCPAP with nasal prongs. High-flow nasal cannula delivered with Vapotherm (VAPO) at 3, 4 and 5 l/min was used. Tidal ventilation was obtained using respiratory inductance plethysmography calibrated with face-mask pneumotachography. An esophageal balloon estimated pleural pressure from which changes in end distending pressure were calculated. Inspiratory, elastic and resistive WOB and respiratory parameters were calculated.

Results

No differences were found in the WOB for all settings. Changes in end distending pressure did not vary significantly over all device settings except VAPO at 5 l/min.

Conclusion

In these preterm infants with mild respiratory illness, HFNC provided support comparable to NCPAP..

Authors	Subject	Publication
Dysart K et al.	Research in high flow therapy: mechanisms of action	Respiratory MEDICINE

REVIEW | VOLUME 103, ISSUE 10, P1400-1405, OCTOBER 01, 2009

Summary

Recently, heater/humidifier devices that use novel methods to condition breathing gases from an external source have been introduced. The addition of sufficient warmth and high levels of humidification to breathing gas has allowed for higher flow rates from nasal cannula devices to be applied to patients (i.e., high flow therapy). This article provides a review of the proposed mechanisms behind the efficacy of high flow therapy via nasal cannula, which include washout of nasopharyngeal dead space, attenuation of the inspiratory resistance associated with the nasopharynx, improvement in conductance and pulmonary compliance, mild distending pressure and reduction in energy expenditure for gas conditioning.

Mechanisms of action for high flow therapy (HFT)

The use of high flow therapy (HFT) devices in clinical settings is rapidly growing. These devices are being applied to patients across age groups in a variety of disease conditions. The mechanisms through which HFT devices affect the respiratory system and alter gas exchange are still under investigation but a growing body of evidence is supporting the mechanisms of action for HFT to be five-fold.

1. HFT provides for washout of nasopharyngeal dead space, which contributes to establishing improved fraction of alveolar gases with respect to carbon dioxide as well as oxygen.¹
2. The distensibility of the nasopharynx provides significant resistance on inspiratory relative to expiratory efforts.² HFT provides adequate flow rates to match inspiratory flow and thus markedly attenuates the inspiratory resistance associated with the nasopharynx, and thus eliminates related work of breathing.
3. The provision of adequately warmed and humidified gas to the conducting airways improves conductance and pulmonary compliance compared to dry, cooler gas.³
4. The provision of adequately warmed and humidified gas through the nasal pharynx reduces the metabolic work associated with gas conditioning.
5. High flow through the nasopharynx can be titrated to provide positive distending pressure for lung recruitment.

Summary

HFT through nasal cannula is now a viable option because of devices that completely warm and humidify inspiratory gases to body temperature and 100% saturation. Properly conditioned gas provides for patient comfort and minimizes deterioration of nasopharyngeal structures. The mechanisms of actions of HFT are five-fold: HFT 1) flushes dead space of the nasopharyngeal cavity allowing for better ventilation as well as oxygenation, 2) provides a flow adequate to support inspiration therefore reducing inspiratory work of breathing, 3) improves lung and airway mechanics by eliminating the effects of drying/cooling, 4) reduces or eliminates the metabolic cost of gas conditioning, and 5) can be used to provide end distending pressure. Numerous studies have shown the safety and efficacy of nasal cannula HFT in the acute care setting, and a number of studies have demonstrated potential for HFT in terms of efficacy beyond conventional oxygenation support

Authors	Subject	Publication
Riemensberger PC et al.	Pediatric and Neonatal Mechanical Ventilation	Springer

Book I © 2015
Pediatric and Neonatal Mechanical Ventilation
From Basics to Clinical Practice

About this book

Written by outstanding authorities from all over the world, this comprehensive new textbook devoted to pediatric and neonatal ventilation puts the focus on the effective delivery of respiratory support to children, infants, and newborns. In the early chapters, developmental issues concerning the respiratory system are considered, physiological and mechanical principles are introduced, and airway management and conventional and alternative ventilation techniques are discussed. Thereafter, the rational use of mechanical ventilation in various pediatric and neonatal pathologies is explained, with the emphasis on a practical step-by-step approach. Respiratory monitoring and safety issues in ventilated patients are considered in detail, and many other topics of interest to the bedside clinician are covered, including the ethics of withdrawal of respiratory support and educational issues. Throughout, the text is complemented by numerous illustrations and key information is clearly summarized in tables and lists, providing the reader with clear "take home messages".

Authors	Subject	Publication
Gausepohl H-J, Pöschl J	Heidelberger Leitfaden Neonatologie 2020	<u>Universtäts Klinikum Heidelberg</u>

(German)
Heidelberger
Leitfaden Neonatologie
2020

Hans-Jürgen Gausepohl und Johannes Pösch

Authors	Subject	Publication
Schmid F et al.	The use of high-flow nasal cannula (HFNC) as respiratory support in neonatal and pediatric intensive care units in Germany – A nationwide survey	Elsevier

Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD00Randomized Controlled Trial J Perinatol. 2006 Aug;26(8):476-80. doi: 10.1038/sj.jp.7211530. Epub 2006 May 11.6405

Abstract

Background

High-flow nasal cannula (HFNC) is a technique of oxygen supply, initially being used as a potentially less-invasive alternative to nasal continuous positive airway pressure (nCPAP) for premature infants/neonates, which nowadays crosses the border of neonatal care. HFNC builds up a positive end-expiratory pressure (PEEP) but lacks the opportunity for continuous monitoring. Therefore, pressure-depending complications are a risk. Our goal was to evaluate the current use of HFNC in Germany regarding indications, techniques of application and complications experienced.

Study design

We used a questionnaire sent to 226 pediatric clinics.

Results

We received responses from 67 pediatric clinics (29.6%). HFNC was applied in the age group of 8 to 14 years in 42% and between 14 and 18 years in 33% of the clinics. 54% of the clinics have been using HFNC for more than 3 years. Applied flow rates varied strongly among the clinics. 70% of the clinics use HFNC outside of the established indications (alternative to nCPAP for premature infants and neonates, bronchiolitis) for pneumonia, support after extubation and non-adherence to nCPAP. Severe complications such as pneumothorax have been seen by 17,9% of the clinics.

Conclusion

We reported for the first time a nationwide overview about the expanded use of HFNC in pediatric clinics. Our results emphasize the fact that, even though HFNC is widely accepted as a non-invasive procedure there is still a potential of severe side effects. Therefore the use of HFNC should be monitored continuously and closely within an intensive or intermediate care unit.

Authors	Subject	Publication
Milési C et al.	High-flow nasal cannula: recommendations for daily practice in pediatrics	Springer

Review | Open Access | Published: 30 September 2014

Abstract

High-flow nasal cannula (HFNC) is a relatively new device for respiratory support. In pediatrics, HFNC use continues to increase as the system is easily set up and is well tolerated by patients. The use of nasal cannula adapted to the infant's nares size to deliver heated and humidified gas at high flow rates has been associated with improvements in washout of nasopharyngeal dead space, lung mucociliary clearance, and oxygen delivery compared with other oxygen delivery systems. HFNC may also create positive pharyngeal pressure to reduce the work of breathing, which positions the device midway between classical oxygen delivery systems, like the high-concentration face mask and continuous positive airway pressure (CPAP) generators. Currently, most of the studies in the pediatric literature suggest the benefits of HFNC therapy only for moderately severe acute viral bronchiolitis. But, the experience with this device in neonatology and adult intensive care may broaden the pediatric indications to include weaning from invasive ventilation and acute asthma. As for any form of respiratory support, HFNC initiation in patients requires close monitoring, whether it be for pre- or inter-hospital transport or in the emergency department or the pediatric intensive care unit.

Authors	Subject	Publication
Lavizzari A et al.	Heated, Humidified High-Flow Nasal Cannula vs Nasal Continuous Positive Airway Pressure for Respiratory Distress Syndrome of Prematurity A Randomized Clinical Noninferiority Trial	JAMA

JAMA Pediatrics | Original Investigation | Journal Club | August 8, 2016

Abstract

Importance

Heated, humidified high-flow nasal cannula (HHHFNC) has gained increasing popularity as respiratory support for newborn infants thanks to ease of use and improved patient comfort. However, its role as primary therapy for respiratory distress syndrome (RDS) of prematurity needs to be further elucidated by large, randomized clinical trials.

Objective

To determine whether HHHFNC provides respiratory support noninferior to nasal continuous positive airway pressure (nCPAP) or bilevel nCPAP (BiPAP) as a primary approach to RDS in infants older than 28 weeks' gestational age (GA).

Design, Setting, and Participants

An unblinded, monocentric, randomized clinical noninferiority trial at a tertiary neonatal intensive care unit. Inborn infants at 29 weeks 0 days to 36 weeks 6 days of GA were eligible if presenting with mild to moderate RDS requiring noninvasive respiratory support. Criteria for starting noninvasive respiratory support were a Silverman score of 5 or higher or a fraction of inspired oxygen higher than 0.3 for a target saturation of peripheral oxygen of 88% to 93%. Infants were ineligible if they had major congenital anomalies or severe RDS requiring early intubation. Infants were enrolled between January 5, 2012, and June 28, 2014.

Interventions

Randomization to either HHHFNC at 4 to 6 L/min or nCPAP/BiPAP at 4 to 6 cm H₂O.

Main Outcomes and Measures

Need for mechanical ventilation within 72 hours from the beginning of respiratory support. The absolute risk difference in the primary outcome and its 95% confidence interval were calculated to determine noninferiority (noninferiority margin, 10%). An intention-to-treat analysis was performed.

Results

A total of 316 infants were enrolled in the study: 158 in the HHHFNC group (mean [SD] GA, 33.1 [1.9] weeks; 52.5% female) and 158 in the nCPAP/BiPAP group (mean [SD] GA, 33.0 [2.1] weeks; 47.5% female). The use of HHHFNC was noninferior to nCPAP with regard to the primary outcome: failure occurred in 10.8% vs 9.5% of infants, respectively (95% CI of risk difference, -6.0% to 8.6% [within the noninferiority margin]; $P = .71$). Significant between-group differences in secondary outcomes were not found between the HHHFNC and nCPAP/BiPAP groups, including duration of respiratory support (median [interquartile range], 4.0 [2.0 to 6.0] vs 4.0 [2.0 to 7.0] days; 95% CI of difference in medians, -1.0 to 0.5; $P = .45$), need for surfactant (44.3% vs 46.2%; 95% CI of risk difference, -9.8 to 13.5; $P = .73$), air leaks (1.9% vs 2.5%; 95% CI of risk difference, -3.3 to 4.5; $P = .70$), and bronchopulmonary dysplasia (4.4% vs 5.1%; 95% CI of risk difference, -3.9 to 7.2; $P = .79$).

Conclusion and Relevance

In this study, HHHFNC showed efficacy and safety similar to those of nCPAP/BiPAP when applied as a primary approach to mild to moderate RDS in preterm infants older than 28 weeks' GA.