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Patient comfort during treatment with heated humidified high flow nasal cannulae versus nasal continuous positive airway pressure: a randomised cross-over trial

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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.

Interventions After parental consent, infants were randomised to 24 h of treatment with NCPAP or HHHFNC followed by 24 h of the alternate therapy.

Main outcome measures Primary outcome was patient comfort assessed by the EDIN (neonatal pain and discomfort) scale. Secondary outcomes were respiratory parameters (respiratory rate, FiO_2, SpO_2, $TcPCO_2$), 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.

ClinicalTrials.gov, number NCT01526226.

What is already known on this topic

- Heated humidified high flow nasal cannulae (HHHFNC) are widely used as respiratory support for preterm infants.
- Despite lack of evidence, heated humidified high flow nasal cannulae (HHHFNC) are presumed to be a gentler mode of non-invasive respiratory support than nasal continuous positive airway pressure (NCPAP).

What this study adds

- Patient comfort on heated humidified high flow nasal cannulae (HHHFNC) and nasal continuous positive airway pressure (NCPAP) was not different using the EDIN scale.
- Respiratory rate was lower on HHHFNC than on NCPAP.
- Parents preferred HHHFNC to CPAP.

INTRODUCTION

The use of heated humidified high flow nasal cannulae (HHHFNC) as a non-invasive mode of respiratory support for preterm neonates has rapidly expanded.[1] Two clinical trials that included preterm infants found HHHFNC comparable with nasal continuous positive airway pressure (NCPAP) in avoiding need for mechanical ventilation and safety.[2 3] The physiological effect of HHHFNC is mediated in part through positive pressure support of the airways, similar to NCPAP, as well as lowering the inspiratory resistance, improvements in conductance and pulmonary compliance and reducing energy expenditure for gas conditioning.[4] The high gas flow, in combination with gas leak around the nostrils, also contributes with dead space washout of CO_2.[1 5]

NCPAP-interfaces, prongs or masks, are strapped tightly to the nose and are often 'bulky'. This may contribute to nasal trauma and impair visual interaction with the child.

Potential benefits of HHHFNC compared with NCPAP include reduced nasal trauma, improved parent interaction[1 6] and reduced ambient noise.[7 8] However, except from a reduction in nasal trauma,[2 3] evidence from clinical trials supporting these benefits is limited.[9] We performed a randomised cross-over trial to test the hypothesis that comfort, defined as absence of prolonged pain, in preterm infants with mild respiratory illness was greater during support with HHHFNC than NCPAP.

METHODS

This study was conducted in the neonatal unit at the University Hospital of North Norway in Tromsø.[10] Infants were eligible for the study if they were less than 34 weeks postmenstrual age (PMA) and had mild respiratory illness defined as treatment with CPAP for at least 72 h if PMA <29 weeks and at least 24 h if 29 weeks to 33 weeks PMA; FiO_2 <0.30; and last (venous/arterial/capillary) PCO_2 <8 kPa before study enrolment. Infants were

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excluded if they were 34 weeks or more PMA, had congenital anomalies, required higher concentrations of supplemental oxygen, or were considered to be in need of frequent blood samples due to infection, hypoglycaemia or other intercurrent conditions. After parental consent, the patients were randomised to continue with NCPAP for 24 h and then switch to HHHFNC for the next 24 h, or to immediately switch to HHHFNC for 24 h and then back to NCPAP for 24 h. After the 48 h study period (2×24 h epochs) further respiratory support was at the discretion of the clinical team.

Equipment

The HHHFNC was administered with the Fisher & Paykel RT329 system (Fisher & Paykel Healthcare, Auckland, New Zealand) using 2.4-mm external diameter nasal cannulae. Gas flow was set at 6 L/min for infants weighing >1500 g and at 5 L/min if <1500 g. The NCPAP was administered using the Infant Flow or SiPAP (CareFusion, San Diego, California, USA) variable flow driver. The nasal interface was either a mask or binasal prongs at the discretion of the nurse. We aimed for a NCPAP of 4–5 cm H_2O. Failure criteria of either HHHFNC or NCPAP during the 48 h study period were a respiratory deterioration with an increase in 1) respiratory rate over first 8 h (>20%), 2) FiO_2 (>0.1) or 3) transcutaneous pCO_2 (>2 kPa), respectively.

Primary and secondary outcomes

The primary outcome was patient comfort, defined as a state free of prolonged pain. Secondary outcomes were respiratory parameters, ambient noise, salivary cortisol and parental assessments of their child.

Patient comfort

This was assessed by a validated neonatal pain and discomfort scale (EDIN scale) that has been in use in our unit since 2007. The EDIN scale is a unidimensional scale using five behavioural indicators (facial activity, body movements, quality of sleep, quality of contact with nurses and consolability) to identify and quantify well-being or prolonged pain in preterm infants.[11 12] Each indicator is scored from 0 to 3 and the EDIN scale is the sum of the five items, that is, final score ranges from 0 to 15. The EDIN score was an assessment over the entire 7–10 h shift (day, evening, night) assigned by the bedside nurse at the end of each shift. For each 24 h period we calculated a cumulative score based on three assessments (day, evening, night).

Respiratory parameters

All patients were monitored with continuous measurement of respiratory rate and SpO_2 throughout the 48 h study period. Values were downloaded from the IntelliVue cardiorespiratory monitoring system (Philips Healthcare, Eindhoven, The Netherlands). Transcutaneous pCO_2 (Radiometer Medical ApS, Brønshøy, Denmark) was measured continuously for the first 2 hours of each 24 h epoch in order to assess whether each of the interventions had an impact of CO_2 removal. FiO_2 values were recorded hourly from the CPAP device or from the oxygen blender for HHHFNC. Target SpO_2 was per unit protocol 90–94% for infants receiving supplemental oxygen.

Ambient noise

Sound levels, expressed in dBA, were measured with a handheld audiometer (Brüel & Kjær, Instr.no: 1648127, Copenhagen, Denmark). The microphone was held approximately 15 cm above the infants face and sound levels were measured twice a day for 10 min during a quiet period in the morning and in the evening. Average sound levels were reported.

Salivary cortisol

Saliva was collected by placing a cotton bud in the patient's mouth for approximately 10 min. Saliva was collected in the morning and evening for each 24 h epoch. We aimed to collect saliva when patients were quiet, fed and comfortable. After collection, the saliva was centrifuged, frozen at −20°C and stored at −70°C. The saliva samples were later analysed with a radioimmunoassay to measure the cortisol concentrations.

Parental assessment

Immediately after each 24 h epoch we administered three questions (box 1) to the parents and asked to respond on a visual analogue scale from 1 to 10. Parents returned the first questionnaire before entering their response for the next 24 h epoch.

Sample size and randomisation

Based on previous observations in our unit we estimated that mean (SD) cumulative EDIN score in infants on NCPAP would be 16 (3). We considered a 25% reduction in the cumulative EDIN score to be clinically relevant. To find this difference with 80% power and a type 1 error of 80%, sample size of 20 infants was required. Infants were block (blocks of 4) randomised, using sealed opaque envelopes, to start with either HHHFNC or CPAP.

Data analysis and statistics

Data were analysed using IBM SPSS (V.20.0) statistical software. Descriptive results are expressed as mean (SD) or median (IQR), as appropriate. Paired t test was used to compare continuous data and proportions were compared using χ^2 test. A $p < 0.05$ was considered statistically significant.

Ethics and trial registration

The study was approved by the committee for human medical research ethics, Region North in Norway. The study was registered with ClinicalTrials.gov (NCT01526226). Written informed consent was obtained from parents before any infant was enrolled in this study.

Results

Forty-six infants with gestational age (GA) <34 weeks were admitted during the study period (February 2012–April 2013). Twenty-one did not meet the inclusion criteria, either due to severe illness or not needing respiratory support. One family was not approached. The parents of 24 infants were approached and all agreed to participate in the study. However, one family withdrew from the study after 24 h HHHFNC not wanting their child back on CPAP. In three infants technical problems led

Box 1 Parental assessment—response on a visual analogue scale 1–10

1. How satisfied do you think your child has been over the last 24 h?
2. How do you assess your contact and interaction with your child over the last 24 h?
3. How do you assess your possibility taking part in nursing and care with your child over the last 24 h?

Table 1 Study population (n=20), baseline data

Gestational age, mean (SD)	29.3 (1.7) weeks
Birth weight, mean (SD)	1234 (353) grams
Postnatal age at study entry, median (IQR)	6 (4–10) days
Last pCO_2 prior to study enrolment*	5.6 (0.9) kPa
Mechanical ventilation prior to study enrolment	6/20 (30%)
Male/female	13/7
Randomised to start with HHHFNC/NCPAP	9/11

*Blood gas obtained during routine clinical care within 96 h prior to study enrolment. No additional blood gases were obtained for study purpose.
HHHFNC, heated humidified high flow nasal cannulae; NCPAP, nasal continuous positive airway pressure.

to exclusion due to missing data. The baseline demographics of the 20 infants included in the study are shown in table 1.

Table 2 shows primary and secondary outcomes. Using the EDIN scale, we found no important differences in patient comfort with HHHFNC versus NCPAP. There was no significant statistical difference in noise with HHHFNC versus NCPAP. Despite our best efforts, we only managed to collect enough saliva for cortisol measurement in 11 out of 80 attempts. Data on cortisol are therefore omitted from statistical comparisons. The parents preferred HHHFNC as respiratory support for their infants. During the 24 h HHHFNC-epoch patients had significantly lower respiratory rate than during the 24 h NCPAP-epoch. All other respiratory parameters were similar. During NCPAP most infants used nasal masks, but some alternated and used masks and prongs during the 24 h epoch. None of the infants met the failure criteria during the study period.

DISCUSSION

In our randomised cross-over trial of preterm infants with mild respiratory illness, patient comfort assessed by bedside nurses using the EDIN scale was comparable on HHHFNC and NCPAP. This is contrary to our hypothesis and to a perception among caregivers that HHHFNC is a gentler means of support.

Among our secondary outcomes, we observed lower respiratory rates in infants on HHHFNC compared with NCPAP. The lower respiratory rate during HHHFNC compared with NCPAP was not reported in a previous clinical study by Saslow *et al* on lung mechanics in neonates during HHHFNC.[13] However, Saslow *et al* only analysed a short observation period (5 min), and infants treated with a flow of 5 L/min actually had a non-significant lower respiratory rate than infants on NCPAP, whereas children treated with lower flow (3 L/min and 4 L/min) had not.[13] Other recent studies in paediatric[14] and adult[15 16] patients have also shown a flow-dependent lower respiratory rate during HHHFNC therapy.[16] There are several putative explanations for the lower respiratory rate during HHHFNC. First, the washout effect of HHHFNC leads to lower CO_2 levels depending on flow and leak.[5] We did not observe differences in $TcPCO_2$ during the two short periods which were analysed in our study. However, a washout effect could have led to a lower respiratory minute volume requirement to control PCO_2, in line with findings from studies in animals[5] and adults.[16] Second, although not supported by our EDIN results, if the child perceives HHHFNC to be less painful than NCPAP, we speculate that this may influence the infant's breathing pattern and lead to a lower respiratory rate.

Finally, we cannot exclude that our HHHFNC therapy with a flow of 5–6 L/min for some infants provided a more powerful respiratory support than a NCPAP of 4–5 cm H_2O.

We found no difference in ambient noise with HHHFNC versus CPAP. However, due to the logarithmic nature of decibel calculations statistical analyses of sound levels needs cautious interpretation. In general, with moderate background sound levels, a 3dBA change may be barely perceptible, a 5dBA change would be readily perceived and a 10dBA difference would be perceived as a doubling of loudness by the human ear.[8]

In this study the parents found that their children were more satisfied during HHHFNC than during NCPAP. Furthermore, they perceived it easier to interact with their child when they were on HHHFNC. The latter finding is of particular interest as improved parent-infant interaction may contribute positively to the development of the child.[17 18] In addition, the fact that the parents found their infants more comfortable and satisfied may be an important factor in reducing parenting stress and anxiety and thereby improve psychological bonding.[19] It is challenging for parents to assess their preference for types of medical support in an unblinded study as their opinions may be influenced by caregivers and other external factors. However, previous studies have shown that parents are able to express clear preferences for respiratory devices used to treat their children.[20]

Our study has several limitations. First, we used our previous observations of EDIN scores in infants on CPAP to estimate our sample size. During the present trial, (average) EDIN scores were substantially lower. Thus, our sample size may have been too small to demonstrate a difference in the two modes of respiratory support. A second limitation is that the EDIN scale, designed to assess pain (high scores), may not be appropriate to assess comfort (low scores). However, in an observational study in preterm infants, type of respiratory support was found to affect the EDIN scale.[12] A third limitation is that in many of our subjects, CPAP was applied using masks rather than nasal prongs. It is possible that masks might be more comfortable than prongs, although we did not record sufficiently detailed data to test that hypothesis. Finally, our study was unblinded and thus subject to potential bias. Although the nurses were asked not to express a preference for either mode of support, it is possible that a positive attitude could be transmitted to the parents. However, the fact that the nurses recorded no difference in the EDIN scale supports our observation that parents independently preferred HHHFNC compared with CPAP.

Table 2 Primary and secondary outcomes

Outcome	HHHFNC	NCPAP	p Value
EDIN score, cumulative*	10.7 (3.3)	11.1 (3.0)	0.35
Noise, dBA	70 (10)	74 (10)	0.18
Parental assessment			
1. Child satisfied	8.6 (1.1)	6.9 (1.6)	<0.001
2. Contact and interaction	9.0 (1.1)	6.7 (1.6)	<0.001
3. Possibility to take part in care	9.1 (1.2)	8.0 (1.6)	0.03
$TcPCO_2$ (mean 2 h) kPa	5.5 (1.1)	5.5 (1.2)	0.87
Respiratory rate (mean 24 h)	41 (7)	46 (9)	0.001
FiO_2 (mean 24 h)	21.8 (1.6)	21.5 (1.1)	0.06
SpO_2 (mean 24 h)	95 (2)	95 (2)	0.41

All data are mean (SD).
*Cumulative score based on assessment over three nursing shifts (day, evening, night).
HHHFNC, heated humidified high flow nasal cannulae; NCPAP, nasal continuous positive airway pressure.

CONCLUSION

In this unblinded, randomised, cross-over trial of infants with relatively mild respiratory illness we found no difference in patient comfort with HHHFNC versus NCPAP using the EDIN

scale. However, parents reported a preference for HHHFNC, and during HHHFNC respiratory rate was significantly lower than during NCPAP.

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Competing interests None.

Patient consent Obtained.

Ethics approval The study was approved by the committee for human medical research ethics, Region North in Norway.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All data from this study, stored in a SPSS file, will be made accessible to other researchers who are interested.

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Notes