Comparison of Effort of Breathing for Infants on Nasal Modes of Respiratory Support

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Objective To directly compare effort of breathing between high flow nasal cannula (HFNC), nasal intermittent mechanical ventilation (NIMV), and nasal continuous positive airway pressure (NCPAP).

Study design This was a single center prospective cross-over study for patients <6 months in the cardiothoracic or pediatric intensive care unit receiving nasal noninvasive respiratory support after extubation. We measured effort of breathing using esophageal manometry with pressure-rate product (PRP) on all 3 modes. NIMV synchrony was determined by comparing patient efforts (esophageal manometry) with mechanically delivered breaths (spirometry in ventilator circuit). On NIMV, PRP and synchrony was also measured after adding a nasal clip on 26 patients.

Results Forty-two children were included. Median (IQR) age was 2 (0.5, 4) months. There was no difference in median PRP between HFNC 6 liters per minute, 355 (270,550), NIMV 12/5 cm H_2O, 341 (235, 472), and NCPAP 5 cm H_2O, 340 (245,506) ($P = .33$). Results were similar regardless of HFNC flow rate or NIMV inspiratory pressure. Median PRP on CPAP of 5 cm H_2O prior to extubation 255 (176, 375) was significantly lower than all postextubation values ($P < .002$). On NIMV, less than 50% of patient efforts resulted in a ventilator breath, which was not improved with a nasal clip ($P > .07$)). However, as NIMV synchrony improved (>60%), PRP on NIMV was lower than on HFNC.

Conclusions For infants, effort of breathing is similar on HFNC, NIMV, and NCPAP after extubation, regardless of flow rate or inspiratory pressure. We speculate that bi-level NIMV may be superior if high levels of synchrony can be achieved. *(J Pediatr 2017;185:26-32).*

Pediatric practitioners use nasal modes of respiratory support such as humidified high flow nasal cannula (HFNC), nasal intermittent mechanical ventilation (NIMV), and nasal continuous positive airway pressure (NCPAP) to improve gas exchange, and work of breathing.[1] Pediatric observational data support lower intubation rates and reduced costs with NCPAP[2] and NIMV.[3-5] These modes are increasingly used after extubation to prevent extubation failure,[6] although pediatric data are sparse.[7-9]

HFNC is sometimes used interchangeably with NCPAP or NIMV. There are few pediatric data comparing clinical outcomes between these 3 nasal modes of respiratory support. Although there are some data comparing physiologic response of each mode,[10,11] existing studies assessing work or effort of breathing are mostly based on subjective clinical scoring systems.[12] We sought to determine if there is a significant difference in objective measures of patient effort of breathing between these modes for infants (<6 months of age) when used after extubation. We hypothesized that NIMV would produce the greatest reduction of effort of breathing, dependent on patient synchrony.

Methods

We conducted a prospective cross-over cohort study in the medical-surgical pediatric intensive care unit (ICU) and cardiothoracic ICU at Children's Hospital Los Angeles from July 2013 until October 2014. The Institutional Review Board at Children's Hospital Los Angeles gave full approval for this study. This was ancillary to a previously published (parent) study, which

CPAP	Continuous positive airway pressure
CPAP 5	CPAP of 5 cm H_2O
HFNC	Humidified high flow nasal cannula
HFNC 6	HFNC 6 liters per minute
ICU	Intensive care unit
NCPAP	Nasal continuous positive airway pressure
NCPAP 5	NCPAP of 5 cm H_2O
NIMV	Nasal intermittent mechanical ventilation
NIMV 12	NIMV with a driving pressure of 12 cm H_2O
NRS	Noninvasive respiratory support
PRP	Pressure-rate product
UAO	Upper airway obstruction

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contains further details about study methodology.[13] Patients were eligible if they were between 37 weeks corrected gestational age and 6 months, intubated >12 hours, had no contraindication to a nasoesophageal catheter or respiratory inductance plethysmoghy bands, and were placed on a nasal mode of respiratory support (HFNC, NIMV, or NCPAP) by the primary team within 1 hour of extubation. Patients on home continuous positive airway pressure (CPAP) or bilevel positive airway pressure were excluded. Informed consent was obtained from the parent/guardian.

We placed an esophageal balloon catheter prior to extubation (Avea SmartCath 6F or 7F, CareFusion, Houten, The Netherlands), respiratory inductance plethysmography bands (Respiband Plus; Viasys Healthcare, Hoechberg, Germany) around the chest and abdomen, and connected a calibrated pneumotachometer (Viasys Variflex 51000-40094; Viasys Healthcare) to the endotracheal tube. Pressure-rate product (PRP), the product of the respiratory rate and peak to trough change in esophageal pressure was measured using previously described methods.[11]

After extubation, HFNC was delivered with an O_2/air blender and a heated humidifier (MR850, Fisher and Paykel Healthcare Limited, Auckland, New Zealand). NIMV and NCPAP were provided either through the Servo-I ventilator system (Servo-I; Maquet, Solna, Sweden) or through the Avea Ventilator System (CareFusion, Yorba Linda, California) using an ICU ventilator equipped with software for air-leak compensation during noninvasive ventilation. To provide NIMV, the Avea was placed in NIMV mode and the Servo-I was placed in NIV pressure control mode, both of which provide time-triggered breaths that are pressure controlled and time cycled. Because both ventilator modes are time triggered this delivers a mandatory breath at a set rate per minute. In addition to time triggering, only the Servo-I in NIV PC mode allows additional flow triggering at the ventilator. However, the additional flow triggering only occurs if the patient is able to generate a sufficiently high peak inspiratory flow rate and the leak at the nasal interface is minimal. Both systems interfaced with the Ram Cannula (NeoTech Products, Valencia, California). For a subset of patients (see below) a nasal clip (Neoseal; NeoTech Products) was added while on NIMV. No proximal trigger device was used, and ventilator settings were not specifically adjusted to improve synchrony.

Prior to extubation, we recorded 5 minutes of steady state spontaneous breathing on CPAP of 5 cm H_2O (CPAP 5), as part of the parent study. After extubation, the choice of using noninvasive respiratory support (NRS) and initial NRS mode was left to the primary team. All patients received HFNC of 4, 6, and 8 liters per minute; NCPAP 5 cm H_2O (NCPAP 5); and NIMV with an expiratory positive airway pressure of 5 cm H_2O, respiratory rate of 20 and a driving pressure (delta P) of 8, 12, and 16 cm H_2O. These settings were chosen based on settings used in previous work, in conjunction with standard ventilator settings used in our ICUs.[14,15] The initial mode of nasal noninvasive ventilation was determined by the clinical team.

Once the patient stabilized on the initial mode, we began the protocol. The sequence of the flow titrations is displayed in **Figure 1** (available at www.jpeds.com). Patients were maintained on each setting for 5-10 minutes prior to study recordings or when switching modes. Measurements were recorded for a minimum of 2 minutes after the patient stabilized on each setting. Patients with upper airway obstruction (UAO) following extubation (as gauged by the UAO tool in the parent study) had recordings postponed until resolution of symptoms, often after administration of racemic epinephrine. We ensured that inspiratory flow limitation was no longer present, and PRP had reached steady state conditions (was no longer changing in response to UAO treatments) before starting measurements. No other respiratory treatments were permitted until the study protocol was complete.

After enrolling 14 patients, we observed low levels of NIMV synchrony and amended the study protocol to test whether addition of a nasal clip device (Neoseal) could achieve better synchrony while patients were on NIMV and reduce effort of breathing. No other changes to the protocol were made to improve synchrony other than the addition of the nasal clip.

Synchrony was quantified by comparing ventilator delivered breaths (by connecting the pneumotachometer through the noninvasive ventilator circuit), with patient efforts (negative deflections in esophageal pressure) with measured recordings taken during 1-minute of steady state breathing. Specifically, we required that ventilator delivered airflow (as measured by spirometry) occurred during the inspiratory phase as defined by continued negative deflections of esophageal pressure. Percent synchrony equals the percentage of ventilator breaths synchronous with patient effort.

Statistical Analyses

Our primary objective was to determine if effort of breathing as measured by PRP was different between HFNC (HFNC 6 liters per minute [HFNC 6]) vs NIMV (NIMV with a driving pressure [delta P] of 12 cm H_2O [NIMV12]) vs NCPAP 5). HFNC 6 and NIMV 12 were used as primary settings for comparisons, as they are commonly used initial settings. Median PRP measured over 2 minutes on HFNC 6 was compared with median PRP on NIMV 12 and median PRP on NCPAP 5 using Friedman ANOVA.

Secondary objectives were to determine how flow rate of HFNC or inspiratory pressure on NIMV changed PRP, and whether these values approximated pre-extubation values on CPAP 5. To do so, we compared median PRP under all study conditions and CPAP 5 with Friedman ANOVA.

Our final objective was to analyze the effects of NIMV synchrony. We compared the percentage of synchronous breaths, stratified by NIMV setting, before and after introduction of the nasal clip using χ^2 tests. We compared PRP, stratified by NIMV setting, before and after introduction of the nasal clip using a Wilcoxon signed rank test. To explore whether NIMV synchrony contributed to a potential improvement in effort of breathing of NIMV over HFNC, we calculated a ratio of PRP on potentially equivalent NIMV and HFNC settings (HFNC 4 was considered equivalent to NIMV 8, HFNC 6 to NIMV 12, and HFNC 8 to NIMV 16). We graphed the ratio of PRP against the percentage of breaths on that NIMV setting