TITLE OF WRITE-UP

MANUSCRIPT CITATION

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Name
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TYPE OF INVESTIGATION
please choose from one of the following: prevention, treatment, diagnosis, prognosis, etiology, quality improvement or continuing medical education, economics of healthcare or interventions, clinical prediction guides, differential diagnosis, systematic review

QUESTION
asked in the study – please state in form of PICOT if appropriate (especially RCT)

METHODS
• Design:
• Allocation: see ACP glossary https://acpj.c.acponline.org/shared/glossary.htm
• Blinding: see ACP glossary
• Follow-up period:
• Setting:
• Patients:. Also include inclusion/exclusion criteria
• Intervention:
• Outcomes:
  o Primary outcome:
  o Secondary outcomes:
• Analysis and Sample Size:
• Patient follow-up: % included in analysis

MAIN RESULTS:
Consider including demographics and details of interest to the reader, potentially in table format.
Can be presented as a table

CONCLUSION:

COMMENTARY:

REFERENCES
Therapy

January 19, 2015

COMMENTARY

Improving rates of extubation failure in very preterm infants remains an important and elusive goal. The importance of this issue is highlighted by the following facts: 1) exposure to and duration of mechanical ventilation is a risk factor for developing bronchopulmonary dysplasia and 2) the diagnosis of bronchopulmonary dysplasia increases the risk of poor neurodevelopmental outcome.(1) Thus, it stands to reason that efforts to minimize exposure to mechanical ventilation will positively impact the long-term outcomes of very preterm infants. Accordingly, the effort to minimize an infant's exposure to mechanical ventilation starts before intubation has even occurred (CPAP vs. prophylactic surfactant,(2) and continues with efforts to optimize successful extubation. Both caffeine and post-extubation CPAP prevent extubation failure and are the standard-of-care for preterm infants. (3,4)

Alternative methods of delivering positive distending pressure to preterm infants, including high-flow nasal cannula (HFNC), are widely used and increasingly popular. The stated and widely accepted advantages of HFNC are ease of use, increased comfort and potential for less nasal trauma. Unfortunately, scant data regarding the risks and benefits of HFNC leaves this practice relatively uninformed. To inform our practice, Manley and colleagues determined whether HFNC performed similarly to nasal CPAP for prevention extubation failure in very preterm infants (<32 wks).(5) This trial was both non-inferiority trial, high-flow nasal cannulae was found to be non-inferior to nasal CPAP for preventing extubation failure.

DELIVERING NON-INVASIVE POSITIVE PRESSURE TO PREVENT EXTUBATION FAILURE IN VERY PRETERM INFANTS: NASAL CPAP REMAINS THE STANDARD OF CARE


Impact ratings: ★★★★★☆

QUESTION

In preterm infants (<32 wks), how does high-flow nasal cannulae compare with nasal CPAP for prevention of extubation failure?

METHODS

Design: Randomized controlled trial
Allocation: Concealed
Blinding: Unblinded (patients, clinicians), Unclear blinding (data collectors, analysts). Impossible to blind patients/clinicians secondary to nature of the intervention.
Follow-up period: Death of first-discharge from hospital (~80 days).
Setting: Three Australian neonatal intensive care units.
Patients: 303 patients, avg. 27.5 wk GA and 1040 g, 53% male, 82% white, 94% received antenatal glucocorticoids, >98% received caffeine prior to extubation, median age of extubation ~40 hrs. Exclusion criteria: >36 wks corrected age at the time of extubation, participation in a concurrent study prohibiting inclusion, major congenital anomaly that might affect breathing, or if maximal intensive care was not being provided.
Intervention: Upon extubation, CPAP (7 cm of water, n=151) or high-flow nasal cannulae (5-6 lpm depending on prong size, n=152). Maximum nasal CPAP administered was 8 cm of water, and maximum high-flow nasal cannulae was 6-8 lpm depending on cannulae size. Infants randomized to receive high-flow nasal cannulae meeting failure criteria were treated with nasal CPAP prior to re-intubation.
Outcomes: The primary outcome was treatment failure within 7 days after extubation. Treatment failure was defined as an FiO2 of 0.2 above baseline value before extubation (goal oxygen saturation 88-92%), pCO2 >60 mmHg, >1 apneic episode requiring intermittent PPV within a 24 hr period or six or more apneic episodes requiring stimulation within 6 consecutive hours or an urgent need for reintubation and mechanical ventilation. Prespecified secondary outcomes included reintubation within 7 days of extubation, requirement for supplemental oxygen at 36 wk gestation, pneumothorax, total days of any respiratory support, duration of oxygen supplementation, length of hospital admission.
Patient follow-up: 100% of the patients randomized were included in the primary analysis.

MAIN RESULT

Treatment failure occurred in 34.2% of those randomized to high-flow nasal cannulae, and 25.8% randomized to CPAP (absolute risk difference 8.4%; 95% confidence interval -1.9 to 18.7).

CONCLUSION

In this non-inferiority trial, high-flow nasal cannulae was found to be non-inferior to nasal CPAP for preventing extubation failure.

COMMENTARY

Improving rates of extubation failure in very preterm infants remains an important and elusive goal. The importance of this issue is highlighted by the following facts: 1) exposure to and duration of mechanical ventilation is a risk factor for developing bronchopulmonary dysplasia and 2) the diagnosis of bronchopulmonary dysplasia increases the risk of poor neurodevelopmental outcome.(1) Thus, it stands to reason that efforts to minimize exposure to mechanical ventilation will positively impact the long-term outcomes of very preterm infants. Accordingly, the effort to minimize an infants' exposure to mechanical ventilation starts before intubation has even occurred (CPAP vs. prophylactic surfactant,(2) and continues with efforts to optimize successful extubation. Both caffeine and post-extubation CPAP prevent extubation failure and are the standard-of-care for preterm infants. (3,4)

Alternative methods of delivering positive distending pressure to preterm infants, including high-flow nasal cannula (HFNC), are widely used and increasingly popular. The stated and widely accepted advantages of HFNC are ease of use, increased comfort and potential for less nasal trauma. Unfortunately, scant data regarding the risks and benefits of HFNC leaves this practice relatively uninformed.

To inform our practice, Manley and colleagues determined whether HFNC performed similarly to nasal CPAP for preventing extubation failure in very preterm infants (<32 wks).(5) This trial was both non-inferiority trial, high-flow nasal cannulae was found to be non-inferior to nasal CPAP for preventing extubation failure.
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practical and clinically relevant. At randomization, the initial HFNC flow rate (5-6 LPM depending on prong size) and CPAP pressure (8 cm H2O) were standardized. From this point forward, clinicians set flow and pressure at their discretion. The authors did not attempt to measure delivered distending pressures as this is rarely, if ever, done clinically. Importantly, this was designed as a non-inferiority trial. In this study, non-inferiority was defined as 20 percentage points above the extubation failure rate for CPAP.

The trial revealed that HFNC was non-inferior to CPAP in preventing extubation failure. Treatment failure occurred in 34.2% of the HFNC group and 25.8% in the CPAP group (risk difference, 8.4 percentage points, 95% confidence interval, -1.9 to 18.7). While this difference did not reach statistical significance, the upper limit of the 95% confidence interval bordered on the margin of non-inferiority. Furthermore, this difference was exaggerated in infants <26 wks gestational age. Specifically, 61.3% of infants <26 wks failed CPAP, while 81.3% of infants failed HFNC. Although the study was not powered to detect differences in this small subgroup of patients (63 infants), based on these data the authors urge caution when considering the use of HFNC in these patients.

Where do these data leave us? Does HFNC perform similarly to CPAP for preventing extubation failure in very preterm infants (<32 wks GA)? Statistically, yes. However, the authors acknowledge that they “chose a generous non-inferiority margin” (6). Ultimately, does HFNC perform well enough compared to CPAP to justify its use to prevent extubation failure? Do these data support using HFNC along side CPAP as the standard of care? As the authors have pointed out, these data clearly argue against the routine use of HFNC following extubation for infants <26 wks. Furthermore, these data provide no compelling argument that HFNC should be considered as equivalent to nasal CPAP as the current standard of care as it relates to preventing extubation failure. However, these data would suggest that HFNC is safe and well tolerated, and warrants further study in the NICU.

References