Discontinuing Nasal Continuous Positive Airway Pressure in Infants ≤32 Weeks of Gestational Age: A Randomized Control Trial

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Objectives To compare immediate cessation of nasal continuous positive airway pressure (NCPAP) vs a stepwise decrease in pressure on the duration of NCPAP therapy in infants born prematurely.

Study design A single center study in infants 23^0-32^6 weeks of gestational age. NCPAP was stopped either at 5 cm H_2O (control) or 3 cm H_2O after a stepwise pressure wean (wean) using defined stability and failure criteria. Primary outcome is total NCPAP days.

Results We enrolled 226 infants; 116 were randomly assigned to control and 110 to the wean group. There was no difference in the total NCPAP days between groups (median [25th, 75th percentiles] 16 [5, 36] vs 14 [7, 33] respectively). There were no differences between groups in secondary outcomes, including duration of hospital stay, critical care days, and oxygen supplementation. A higher proportion of control infants failed the initial attempt to discontinue NCPAP (43% vs 27%, respectively; $P < .01$) and required ≥2 attempts (20% vs 5%, respectively; $P < .01$). In addition, infants 23-27 weeks of gestational age in the wean group were 2.4-times more likely to successfully stop NCPAP at the first attempt ($P = .02$) vs controls.

Conclusions Discontinuation of NCPAP after a gradual pressure wean to 3 cm H_2O did not decrease the duration of NCPAP therapy compared with stopping from 5 cm H_2O in infants ≤32 weeks of gestational age. However, weaning decreased failed initial attempts to stop NCPAP, particularly among infants <28 weeks of gestational age. *(J Pediatr 2021;230:93-9)*.

Trial registration Clinicaltrials.gov: NCT02064712.

Nasal continuous positive airway pressure (NCPAP) is a mainstay of respiratory support for infants born prematurely.[1,2] Application of NCPAP soon after birth decreases the need for mechanical ventilation, improves mortality, and decreases the occurrence of bronchopulmonary dysplasia (BPD).[3] In addition, NCPAP is used for postextubation respiratory support[4] and treatment of apnea of prematurity[5] and evolving or established BPD.[6] Despite its wide use, the optimal method for discontinuing NCPAP therapy in infants born prematurely remains unclear. Early discontinuation has been associated with increased apnea, atelectasis, increased work of breathing, and hypoxic events,[7] and longer duration of oxygen therapy and respiratory support.[8] However, NCPAP therapy is associated with an increased risk for nasal septal injury,[9] pneumothorax,[10] gastric distension,[11] delayed initiation of oral feeding, and increased patient discomfort.[12,13] An optimal strategy for discontinuing NCPAP is necessary to decrease the duration of NCPAP therapy without increasing adverse events.

Four main methods of discontinuing NCPAP have been studied, including sudden stopping from a predetermined level, gradual time cycling,[14-16] gradual pressure wean,[17-20] and weaning from NCPAP to high flow nasal cannula.[8,21] Compared with sudden stopping, gradual cycling time off NCPAP has led to longer duration of NCPAP therapy, respiratory support, hospital stay, and higher incidence of BPD.[14] Similarly, early weaning of NCPAP 5 cm H_2O and fraction of inspired oxygen (FiO_2) ≤0.3 to high flow nasal cannula at 2 liter/minute has resulted in longer duration of supplemental oxygen therapy and respiratory support compared with continued NCPAP therapy until reaching $FiO_2 = 0.21$.[8] To date, only 2 studies have compared sudden stopping with a gradual pressure wean. In a single center study of 68 infants, Amatya et al observed fewer failed discontinuation attempts in infants 26-31 weeks of gestational age after a gradual wean approach to 3 cm H_2O compared with sudden stopping from a level of 5 cm H_2O.[17] In a multicenter study that included 344 infants, Jensen et al examined the effect of stopping NCPAP at <8 cm H_2O vs a gradual pressure wean to 4 cm H_2O on weight gain velocity.[18] Although they observed no difference in the primary outcome, infants <28 weeks of gestational age were more likely to have NCPAP discontinued on the first attempt after gradual weaning.[18]

The primary aim of this study was to compare the total duration of NCPAP therapy after a gradual pressure wean to 3 cm H_2O vs stopping at the therapeutic level of ~5 cm H_2O. We hypothesized that in the presence of well-defined failure criteria,

BPD	Bronchopulmonary dysplasia
CPAP	continuous positive airway pressure
FiO_2	Fraction of inspired oxygen
NCPAP	Nasal continuous positive airway pressure
NICU	Neonatal intensive care unit
PMA	Postmenstrual age
RCT	Randomized controlled trial

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infants ≤32 weeks of gestational age undergoing a progressive wean in NCPAP pressure from 5 to 3 cm H_2O would have fewer total NCPAP days vs those removed from NCPAP at 5 cm H_2O.

Methods

Study Design

This is a single center unblinded prospective randomized controlled trial (RCT) conducted in the Parkland Hospital neonatal intensive care unit (NICU) in Dallas, TX. Infants 23^0-32^6 weeks of gestational age requiring NCPAP or mechanical ventilation with the intention of extubation were eligible for enrollment. We excluded infants with congenital anomalies, severe intraventricular hemorrhage, need for surgery, requiring transfer to another center, and those receiving NCPAP <48 hours.

Setting and Participants

Parkland Hospital is a large public hospital in Dallas County, Texas with >12 000 deliveries annually. There is a dedicated "resuscitation team" that attends all high-risk deliveries. All infants ≤32 weeks of gestational age with any respiratory distress are immediately placed on continuous positive airway pressure (CPAP) using a T-Piece resuscitator (Neopuff, TM Fisher and Paykel). Face mask positive pressure ventilation is provided as indicated by Neonatal Resuscitation Program guidelines.[22] Intubation is restricted to infants not responding to positive pressure ventilation. Infants stabilized on face mask CPAP are switched to bi-nasal prongs (Hudson Prongs, Hudson RCI) connected to a positive end expiratory pressure valve with a flow of 8-10 liter/minute before transport to the NICU. Upon admission to the NICU, infants are placed on bubble NCPAP (Fisher and Paykel Healthcare, Auckland, New Zealand). Those requiring FiO_2 ≥0.45 on NCPAP of 6-7cm H_2O are intubated, mechanically ventilated, and administered surfactant soon after intubation. NCPAP levels of 5-8 cm H_2O are used routinely for postextubation respiratory support. Regular training of nurses and respiratory therapists together with bedside auditing of the NCPAP delivery system were conducted throughout the study period.[23] Oxygen saturation was maintained at 88%-94% throughout the NICU stay. All infants born <30 weeks of gestational age are routinely started on caffeine on admission and continued until they have no apnea events for ≥7 days or at 34 weeks of postmenstrual age (PMA).

Study Intervention

The primary care team managed all consented infants until they met entry criteria of NCPAP of 5 cm H_2O and FiO_2 <0.25, at which time they were eligible for weaning after meeting the 24 hours stability criteria described in **Table I**. The details of the weaning process are described in **Figure 1** (available at www.jpeds.com). NCPAP was stopped at 5 cm H_2O in the control group. In the wean group, NCPAP was decreased progressively every 24 hours to a value of 3 cm H_2O, at which time NCPAP was removed and the neonate given a trial off therapy. NCPAP level could be increased back to the previous pressure level if a neonate met failure criteria after a decrease in pressure. If there was an oxygen requirement before or after stopping NCPAP, infants were placed on a low flow nasal cannula (at 1 liter/minute). If a neonate met failure criteria, NCPAP was restarted at 5 cm H_2O in the control group and 3-5 cm H_2O in the wean group as described. This cycle was repeated until the neonate was stable for 5 days off NCPAP, at which time they were considered successfully weaned. All study infants were followed until hospital discharge, at which time the primary and secondary outcomes were determined.

Table I. Stability and failure criteria for weaning NCPAP

Stability criteria: (must meet all criteria for minimum of 24 h)
- NCPAP 5 cm H_2O
- Supplemental FiO_2 <0.25 and not increasing
- Respiratory rate ≤60 breaths/min
- No significant respiratory distress (eg, retractions, dyspnea)
- <3 episodes of apnea (>20 s) with bradycardia (<100 beats/min) and/or desaturations (<88%) within 1 h or <5 episodes in the prior 12 h
- Average oxygen saturation 88%-94% with stable FiO_2
- Tolerate time off NCPAP during routine care procedures
- Neonates <27 wk of gestational age must be ≥10 d postnatal before weaning

Failure criteria:
- ≥3 apneas with bradycardia and/or desaturations in 1 h or >4 episodes in a 12-h period
- Increasing need for FiO_2 >0.3 to maintain oxygen saturation 88%-94%
- Increase in P_aCO_2 >65 mm Hg
- Increased work of breathing with respiratory rate >75 breaths/min for >2 h
- Apnea requiring resuscitation or extensive/vigorous stimulation
- Initiation of nasal intermittent positive pressure ventilation for respiratory support

Outcomes

The primary outcome was the total days of NCPAP therapy. A NCPAP day was defined as the need for any NCPAP support in a 24-hour period. Secondary outcomes included days of supplemental oxygen defined as any supplemental oxygen for 12 consecutive hours in a 24-hour period, duration of hospital days, and number of failed stopping attempts. Restarting NCPAP within 5 days of cessation was considered a failed stopping attempt. BPD was defined as the need for supplemental oxygen at 36 weeks of PMA,[24,25] which was further confirmed by timed oxygen reduction test in select group of patients per standard guidelines.[26] Severe intraventricular hemorrhage was any grade III-IV hemorrhage on cranial ultrasound.[27] Severe retinopathy of prematurity was stage 3 or greater based on the international classification of retinopathy.[28]

The Institutional Review Board of University of Texas Southwestern Medical Center and Parkland Health and Hospital Systems approved the trial. Informed consent was obtained from parents before enrollment of each neonate. The study is registered in ClinicalTrials.gov identifier: NCT02064712.

Infants were randomized using serial computer generated sequence with a ratio of 1:1 between the control and wean groups. Randomization sequences were generated by a statistician and were placed in an opaque envelope by nonstudy personnel. Envelopes were opened in sequential order by the study team members after each neonate was enrolled.

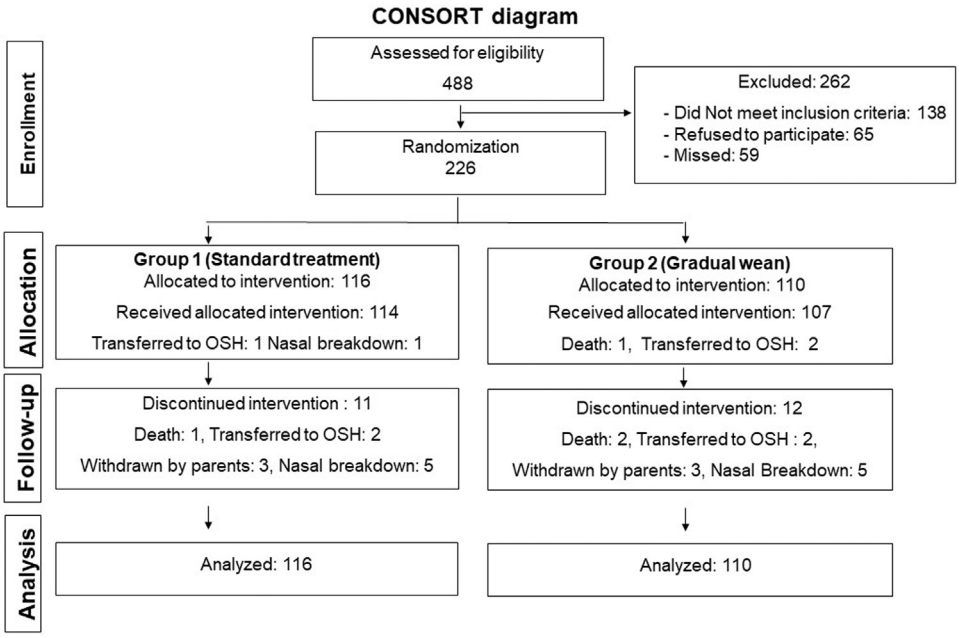

Figure 2. CONSORT diagram.

Statistical Analyses

To assess the number of infants needed in each arm, we examined NCPAP use between 2009 and 2012 in a validated database maintained for NICU patients for the past 40 years. In total, 471 infants ≤32 weeks of gestational age were delivered during that time and required NCPAP >2 days, mean total NCPAP days 15.3 ± 14 (SD). To reduce the total NCPAP days by 25% (ie, ~3.8 days), the sample size needed for a power of 0.80 and significance level alpha of 0.05 was 113 in each arm or 226 total.

Patient demographics are presented using proportions, means ± SDs or medians (25th, 75th percentiles) and ranges. A descriptive analysis of the primary endpoint (ie, the number total NCPAP days was performed). The primary endpoint was compared between groups using the Mann-Whitney U test or *t* test depending on the data distribution. All other continuous variables used the appropriate test dependent on data distribution. Proportions were compared between groups using the χ^2 test. A post hoc subgroup analysis of infants 23-27 weeks of gestational age and 28-32 weeks of gestational age was conducted applying similar statistical methods. Secondary analyses were performed using similar statistical methods. All statistical tests used an $\alpha = 0.05$.

Results

We screened 488 infants and consented and enrolled 226 between September 2014 and February 2018. Of these, 116 were randomly assigned to the control group and 110 to the wean group. Nineteen control infants and 21 wean infants had protocol violations (**Figure 2**). All enrolled infants were included in the intention-to-treat analysis. There were no differences in the baseline demographics between the treatment groups, including ethnicity, exposure to antenatal steroids, mode of delivery, sex, and gestational age. In addition, there was no difference in the proportion of infants receiving mechanical ventilation and ventilator days between 2 groups (**Table II**).

At initiation of the study, there were no significant differences between control and wean infants in postnatal age at the introduction of NCPAP, age of randomization, or number of days on NCPAP before meeting study entry criteria and before the first wean attempt (**Table III**). The primary outcome, total number of days on NCPAP, was not different between the 2 treatment groups. Similarly, there were no differences in any of the secondary outcomes (duration of supplemental oxygen, length of hospital stay, or number of critical care days, **Table III**). The control group was nearly twice as likely to fail the first attempt to stop NCPAP ($P = .01$) and 4 times more likely to have failed ≥2 attempts to stop NCPAP ($P < .01$). There was no difference in the weight gain velocity between the study groups or the occurrence of morbidities such as pneumothorax, BPD, need for postnatal steroid, severe retinopathy, and mortality between 2 groups (**Table III**).

To determine if there were gestational age-dependent variables related to the success of stopping NCPAP therapy, we performed post hoc subgroup analysis, using 23-27 weeks of gestational age and 28-32 weeks of gestational age. As with the total groups, there were no differences in the primary outcome in either gestational age group (**Tables IV** and **V**; available at www.jpeds.com). Nonetheless, a greater number of control infants 23-27 weeks of gestational age failed the initial attempts to stop NCPAP compared with infants in the wean group.

We examined the reasons for the failed attempts to stop NCPAP therapy. There were 131 failed attempts, 44% were

Table II. Maternal and neonatal characteristics in control and wean study groups prior to initiation of study intervention

Characteristics	Control (n = 116)	Wean (n = 110)	*P* value
Maternal:			
Age (y)	28 ± 8*	29 ± 7	.25
Racial/ethnic groups			
White non-Hispanic	4 (3)†	7 (6)	.65
African American	30 (26)	30 (27)	
Hispanic	81 (70)	71 (65)	
Other	1 (1)	2 (2)	
Gravity	3 ± 2	3 ± 2	.46
Preeclampsia	48 (41)	43 (39)	.73
Antenatal steroids	90 (78)	87 (79)	.78
Multiple births	26 (22)	34 (31)	.15
Cesarean delivery	85 (73)	87 (79)	.31
Neonatal:			
Male	64 (55)	56 (51)	.52
Gestational age (wk)	28 ± 2	29 ± 2	.70
Birth weight (g)	1229 ± 397	1257 ± 380	.58
Apgar scores			
1 min	5 (2, 7)‡	5 (2, 6)	.62
5 min	7 (6, 8)	7 (5, 8)	.26
Admitted on NCPAP	88 (76)	79 (72)	.49
Surfactant therapy	66 (57)	67 (61)	.54
Requiring mechanical ventilation	52 (45)	51 (46)	.82
Age NCPAP started (d)	0 (0, 5)	0 (0, 6)	.66
Maximum NCPAP (cm H_2O)	6 (5, 7)	6 (6, 7)	.52
Ventilator days	3 (1, 9)	3 (1, 12)	.56
Pneumothorax	9 (8)	8 (7)	.89

*Values are means ± SD. Data analyzed by nonpaired *t* test.
†Values in parentheses are the percent of the total number in each column. Data analyzed by χ^2 test.
‡Values are medians with 25th, 75th percentiles. Data analyzed by Mann-Whitney U test.

due to increased apneic episodes, 29% due to increased respiratory distress associated with tachypnea or increased work of breathing, and 27% due to decreases in oxygen saturation that required increases in supplemental oxygen (ie, FiO_2 ≥0.3). Seven (5%) infants who failed NCPAP cessation underwent a sepsis evaluation, and 3 (2%) required intubation and initiation of mechanical ventilation.

Discussion

In this single center RCT, we did not find differences in the total duration of NCPAP therapy, duration of oxygen therapy, or hospital for infants who had therapy immediately stopped at a pressure of 5 cm H_20 vs those who underwent a gradual pressure wean to 3 cm H_20. However, a higher proportion of control infants failed the first attempt to stop NCPAP and were more likely to require 2 or more attempts to successfully stop NCPAP therapy compared with infants undergoing a gradual pressure wean.

Our study findings are consistent with 2 previous studies that compared the sudden cessation of NCPAP with a gradual pressure wean. Amatya et al observed a higher rate of failed initial stopping attempts after stopping at 5 cm H_2O compared with 3 cm H_2O, but no difference in the total NCPAP days or PMA at which NCPAP therapy was stopped.[17] Gestational age stratification was not performed due to the small study population. Jensen et al reported no difference in duration of weaning of NCPAP therapy between sudden stopping at ≤7 cm H_2O and gradually weaning to 4 cm H_2O, however, they observed higher rate of failed stopping attempts after stopping at the higher pressure among infants <28 weeks of gestational age.[18]

We chose the primary outcome of total NCPAP days because of its potential impact on several short-term outcomes. Zhang et al observed higher lung volume and strain induced lung growth among ferrets in the presence of CPAP compared with atmospheric pressure for 2 weeks.[2] Lam et al reported a higher functional residual capacity when NCPAP was applied for 2 weeks beyond the point of meeting stability criteria in infants ≤32 weeks.[29] Anecdotal experiences also suggest that longer duration of NCPAP therapy is associated with lower incidence of BPD.[30,31] However, prolonged NPCAP could also result in numerous adverse events such as nasal septal injury,[9] delayed initiation of oral feeding,[32] patient discomfort,[33] interference with parental bonding,[34,35] and increased resource utilization.

To date, studies comparing different methods of weaning NCPAP have provided conflicting results. One multicenter trial reported shorter duration of NCPAP therapy with sudden stopping compared with gradual cycling time off.[14] Two single center studies reported decreased duration of NCPAP therapy with gradual pressure weaning compared with gradual cycling time off.[19,20] Moreover, a meta-analysis suggested that sudden discontinuation results in discontinuation of NCPAP at lower PMA, but at the expense of higher failed stopping attempts.[36] Although progressive weaning might prolong the duration of the weaning process,[12] we hypothesized that a gradual stepwise decrease in pressure would decrease the duration of NCPAP therapy by preventing repetitive cycles of atelectasis and re-expansion that might be associated with stopping NCPAP at higher pressures.[37] However, the method of weaning did not affect the total duration of therapy, despite control group having shorter wean duration.

The decision to either stop or wean NCPAP pressure is often based on the anecdotal experience of the caregiver. To establish a consistent, reproducible approach based on physiologic criteria, we employed the clinical stability and failure criteria reported by Todd et al.[14] However, we made 3 modifications: (1) the level of NCPAP pressure in the control group was set at 5 cm H_2O vs a range of 4-6 cm H_2O; (2) the minimum age to qualify for cessation or weaning was set at 10 days of age for infants <26 weeks of gestational age; and (3) when a neonate required supplemental oxygen, we allowed use of nasal cannula for the delivery of oxygen at 1 liter/minute after stopping NCPAP, which provides no significant airway pressure.[30] In the present report, there were no differences between study groups in the age at which infants were first weaned, suggesting the stability criteria were consistently applied in both study groups. Of those infants who failed the initial attempt to stop NCPAP, only 3 required intubation and mechanical ventilation and the majority responded to restarting NCPAP. This also supports the conclusion that use of standardized stability and failure criteria provided safe measures for weaning infants born prematurely from NCPAP, consistent with the previous studies.[14,18]

Table III. Comparison of clinical status of all neonates randomized to control and wean groups at entry to the study, at the time of first NCPAP wean/cessation, and responses to weaning

Clinical status	Control group (n = 116)	Wean group (n = 110)	*P* value
Postnatal age at randomization (d)	2 (1, 5)*	2 (1, 3)	.39
Days of NCPAP before meeting entry criteria	6 (3, 16)	5 (2, 8)	.29
Characteristics at first wean:			
Postnatal age (d)	11 (6, 35)	9 (5, 24)	.40
PMA (wk)	31 (30, 32)	31 (30, 32)	.54
Days of NCPAP before (d)	9 (5, 26)	7 (4, 18)	.14
Time from randomization (d)	6 (3, 24)	6 (2, 19)	.31
Weight (g)	1477 ± 388†	1450 ± 325	.58
Characteristics at first attempt to stop NCPAP:			
PMA (wk)	31 (30, 32)	32 (31, 33)	<.01
Days of NCPAP before (d)	9 (5, 26)	12 (7, 25)	.03
Weight (g)	1477 ± 388	1564 ± 346	.08
Primary outcome:			
Days of NCPAP at final cessation	16 (5, 36)	14 (7, 33)	.56
Days of NCPAP in mechanically ventilated infants	28 (9, 41)	21 (10, 48)	.85
Days of NCPAP in nonmechanically ventilated infants	9 (4, 22)	10 (6, 22)	.32
Secondary outcomes:			
PMA at cessation of NCPAP (wk)	32 (31, 33)	32 (31, 34)	.23
Days of NCPAP from first wean to cessation (d)	0 (0, 9)	5 (2, 13)	<.01
Weight at cessation of NCPAP (m)	1618 ± 427	1651 ± 380	.55
Neonates failing first attempt to stop NCPAP	50 (43)‡	30 (27)	.01
Neonates failing ≥2 attempts to stop NCPAP	23 (20)	5 (5)	<.01
Duration of supplemental oxygen (d)	26 (4, 56)	21 (3, 54)	.63
Critical care days (d)	25 (10, 49)	22 (10, 49)	.93
Length of hospital stay (d)	68 (44, 97)	66 (47, 87)	.45
PMA at initiation of oral feedings (wk)	34 (33, 35)	34 (33, 35)	.79
Weight gain velocity during weaning (g/d)	20 (16, 29)§	20 (9, 29)	.33
Complications:			
BPD	14 (12)	15 (14)	.73
Postnatal steroid	5 (16)	2 (7)	.43
Severe retinopathy (≥stage 3)	7 (6)	5 (5)	.66
Mortality	2 (2)	2 (2)	1.00

*Values are medians (25th, 75th percentiles). Data analyzed by Mann-Whitney U test.
†Values are means ± SD. Data analyzed by nonpaired *t* test.
‡Values are the number of patients, and parentheses are the percent of the number in each column. Data analyzed by χ^2 test.
§Average weight gain from day of first wean to day of cessation of NCPAP. Values are medians with 25th, 75th percentiles. Data analyzed by Mann-Whitney U test.

We employed a low NCPAP pressure in our weaning strategy, which is similar to that used by Amatya et al.[17] NCPAP pressures of 3-4 cm H_2O have been shown to improve functional residual capacity, increase inspiratory effort, and decrease supraglottic resistance and episodes of obstructive apnea.[5,38-41] Moreover, 3 cm H_2O of NCPAP pressure also decreases thoracoabdominal asynchrony and work of breathing, aiding in overcoming a high respiratory load.[40-42] We believe that a gradual wean to 3 cm H_2O may also condition the respiratory muscles and aid in the successful transition off NCPAP. This may have contributed to fewer failed attempts to stop NCPAP in the wean group, particularly among infants born <28 weeks of gestational age.

The number of failed initial stopping attempts observed in our study is similar to other studies. Amatya et al reported that 60% of infants failed first stopping attempt in the sudden stopping arm compared with 34% in the gradual pressure wean arm.[17] Similarly, 55% of infants studied by Jensen et al failed NCPAP in the sudden stopping arm compared with 47% in the gradual pressure wean group.[18] The failed stopping attempts in our study were primarily due to increased apnea and an increased need for supplemental oxygen. Although the majority of infants in our study recovered after replacing the NCPAP, these events could lead to escalation of support including intubation, initiation of septic work up, and antibiotic therapy. Our study demonstrates that gradual pressure weaning guided by well-defined stability and failure criteria facilitate successful cessation of NCPAP in infants born prematurely without prolonging the duration of therapy.

Our study has several limitations. It was unblinded and weaning decisions could have been affected by the biases of the clinical care team. However, a large group of providers participated in the care of the study infants throughout the study period thereby mitigating a systematic bias. Our study also did not specify the strategy to wean NCPAP from levels >5 cm H_2O or when to stop noninvasive positive pressure ventilation, which could have affected the total duration of NCPAP. However, there were no significant differences in the number of NCPAP days prior to meeting entry criteria or the initiation of weaning in 2 groups. Although there was a time lag between patient randomization and initiation of the intervention, which could potentially lead to bias between groups, there was no difference in the time to initiate weaning from the time of enrollment between 2 groups. Finally, 10% of infants in each arm of the study did not complete the study. However, the final analyses showed no differences in the total duration of NCPAP therapy in the 2 arms and the inclusion of more infants would not have changed the outcome.

Our study also has several strengths. We compared NCPAP cessation at a high, set therapeutic pressure with gradual pressure wean to a much lower value, 5 vs 3 cm H_2O, and included a relatively large proportion of infants <28 weeks of gestational age. The higher failure rate for stopping attempts in the control group suggests that a gradual wean to lower pressure is beneficial in identifying infants who are most likely to succeed at discontinuation of NCPAP Finally, our study initiated the weaning process using stability criteria independent of postnatal age, which may be more physiologic. Our study findings suggest that infants <32 weeks of gestational age can be successfully weaned using stability criteria alone.

In conclusion, in this single center RCT, cessation of NCPAP at 5cm H_2O pressure vs a gradual pressure wean from 5 to 3cm H_2O had no effect on the total duration of NCPAP therapy in infants ≤32 weeks of gestational age. However, weaning NCPAP pressure to 3 cm H_2O significantly decreased the number of failed initial attempts to stop NCPAP, especially in infants <28 weeks of gestational age. ■

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50 Years Ago in *The Journal of Pediatrics*

Vigorous and Repeated Nasopharyngeal Suctioning

Cordero L, Hon EH. Neonatal bradycardia following nasopharyngeal stimulation. J Pediatr 1971;78:441-7.

Fifty years ago in *The Journal of Pediatrics*, Cordero and Hon described responses in 41 infants who were suctioned in the oro-/nasopharynx with a bulb syringe and 46 infants suctioned with a 5- or 8-Fr feeding tube and a de Lee trap. Suctioning with a bulb syringe did not cause bradycardia, whereas prolonged suctioning with a feeding tube caused bradycardia in 7 (15%), and apnea in 5 (11%) infants. Two required intubation, one of whom experienced cardiac arrest and received chest compressions.

Cordero and Hon were cited in the American Heart Association/International Liaison Committee on Resuscitation 2000 guidelines[1]; however, not until 2010, routine oro/pharyngeal suctioning was discouraged due to concerns that the harm might outweigh the theoretical benefits of facilitating lung fluid clearance.[2] A 2017 Cochrane review including 8 (quasi-) randomized trials showed no difference in intubation, oxygen, chest compression, or adrenaline administration between routine oro-/nasopharyngeal suctioning vs no suction.[3] Cordero and Hon's study was excluded, as it was nonrandomized. No study reported the outcomes arrhythmia or apnea, but oxygen saturation was different, favoring no suction initially. However, after 15-20 minutes, oxygen saturation became greater in the suctioned infants.

The risk of bias of nonrandomized observations might be an explanation why serious adverse events could not be confirmed by the Cochrane review. Cordero and Hon reported intrapartum oral and nasal suctioning followed by 10-20 seconds of blind suctioning after birth. Such repeated and vigorous suctioning belongs to the past and should be avoided.

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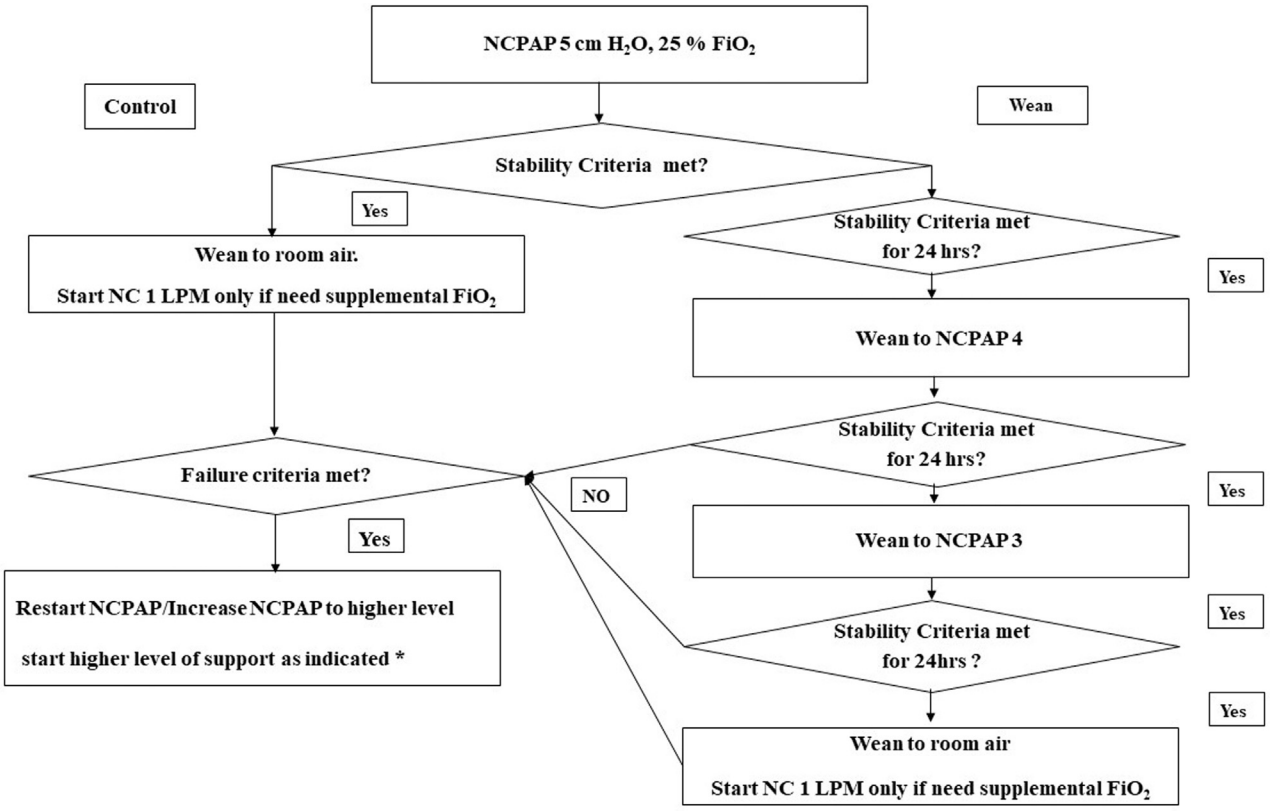

Figure 1. NCPAP weaning algorithm. *NC 1LPM*, nasal cannula 1 liter per minute.

Table IV. Comparison of clinical status of control and wean groups in neonates born at 23-27 weeks of gestational age at entry to the study, at the time of first NCPAP wean/cessation, and responses to weaning

Clinical status	Control group (n = 43)	Wean group (n = 35)	*P* value
Postnatal age at randomization (d)	4 (2, 11)§	3 (1, 15)	.52
Days of NCPAP before meeting entry criteria	19 (7, 31)	14 (4, 32)	.37
Characteristics at first wean:			
Postnatal age (d)	41 (24, 60)	40 (24, 57)	.71
PMA (wk)	32 (30, 34)	32 (30, 33)	.53
Days of NCPAP (d)	27 (14, 41)	25 (10, 43)	.66
Time from randomization (d)	31 (15, 40)	30 (9, 43)	.94
Weight (m)	1469 ± 510*	1473 ± 418	.97
Characteristics at first attempt to stop NCPAP:			
PMA (wk)	32 (30, 34)	33 (31, 35)	.15
Days of NCPAP before (d)	27 (14, 41)	38 (24, 52)	.04
Weight (g)	1469 ± 510	1685 ± 423	.07
Primary outcome:			
Days of NCPAP at final cessation	36 (21, 47)	43 (21, 55)	.41
Days of NCPAP in the Mechanically ventilated infants	38 (25, 46)	44 (14, 57)	.51
Days of NCPAP in the nonmechanically ventilated infants	35 (17,50)	33 (23, 52)	.45
Secondary outcomes:			
PMA at cessation of NCPAP (wk)	33 (32, 35)	33 (32, 35)	.39
Days of NCPAP from first wean to cessation (d)	4 (0, 13)	11 (4, 20)	<.01
Weight at cessation of NCPAP (g)	1693 ± 588	1835 ± 463	NS
Neonates failing first attempt to stop NCPAP	24 (56)†	10 (29)	.02
Neonates failing ≥2 attempts to stop NCPAP	12 (28)	2 (6)	.01
Duration of supplemental oxygen (d)	60 (38, 96)	61 (36, 92)	.61
Critical care days (d)	51 (39, 76)	56 (35, 80)	.69
Length hospital stay (d)	102 (93, 125)	102 (81, 124)	.62
PMA at initiation of oral feedings (wk)	34 (33, 36)	34 (33, 36)	.89
Weight gain velocity during weaning (g/d)	24 (16, 35)‡	28 (20, 31)	.61
Complications:			
BPD	12 (28)	11 (31)	.73
Postnatal steroid	5 (18)	2 (10)	.68
Severe retinopathy (≥stage 3)	6 (27)	5 (26)	.05
Mortality	2 (5)	2 (6)	1.0

*Values are means ± SD. Data analyzed by nonpaired *t* test.
†Values number of patients and parentheses are the percent of the number in each column. Data analyzed by χ^2 test.
‡Average weight gain from day of first wean to day of cessation of NCPAP.
§Values are medians with 25th, 75th centiles. Data analyzed by Mann-Whitney U test.

Table V. Comparison of clinical status of control and wean groups in neonates born at 28-32 weeks of gestational age at entry to the study, at the time of first NCPAP wean/cessation, and responses to weaning

Clinical status	Control group (n = 73)	Wean group (n = 75)	*P* value
Postnatal age at randomization (d)	2 (1, 3)§	2 (1, 3)	.80
Days of NCPAP prior to meeting entry criteria	4 (2, 6)	4 (2, 7)	.79
Characteristics at first wean			
Postnatal age (d)	6 (4, 11)	7 (4, 10)	.85
PMA (wk)	31 (30, 32)	31 (30, 32)	.76
Days of NCPAP (d)	6 (3, 10)	5 (4, 8)	.81
Time from randomization (d)	4 (2, 8)	4 (2, 8)	.65
Weight (g)	1482 ± 308*	1441 ± 279	.40
Characteristics at first attempt to stop NCPAP:			
PMA (wk)	32 (30, 34)	33 (31, 35)	.15
Days of NCPAP (d)	6 (4, 10)	9 (6, 13)	<.01
Weight (g)	1482 ± 308	1515 ± 300	.50
Primary outcome			
Days of NCPAP at final cessation	7 (4, 20)	10 (6, 19)	.08
Days of NCPAP in the mechanically ventilated infants	13 (6,29)	18 (8,23)	.40
Days of NCPAP in the nonmechanically ventilated infants	6(4,18)	9 (6,17)	.10
Secondary outcomes			
PMA at cessation of NCPAP (wk)	32 (31, 33)	32 (31, 33)	.18
Days of NCPAP from first wean to cessation (d)	0 (0, 7)	4 (2, 11)	<.01
Weight at cessation of NCPAP (g)	1579 ± 309	1578 ± 316	.97
Neonates failing first attempt to stop NCPAP	26 (36)†	20 (27)	.24
Neonates failing ≥2 attempts to stop NCPAP	11 (15)	3 (4)	.02
Duration of supplemental oxygen (d)	12 (2, 27)	7 (2, 31)	.74
Critical care days (d)	12 (8, 26)	13 (9, 24)	.43
Length of hospital stay (d)	56 (39, 69)	54 (41, 67)	.75
PMA at initiation of oral feedings (wk)	33 (33, 34)	34 (33, 35)	.67
Weight gain velocity during weaning (g/d)	20 (13, 27)‡	16 (1, 25)	.28
Complications:			
BPD	2 (3)	4 (5)	.68
Postnatal steroid	0 (0)	0 (0)	
Severe retinopathy (≥stage 3)	1 (14)	0 (0)	1.00
Mortality	0 (0)	0 (0)	

*Values are means ± SD. Data analyzed by nonpaired *t* test.
†Values are number of patients and parentheses are the percent of the number in each column. Data analyzed by χ^2 test.
‡Average weight gain from day of first wean to day of cessation of NCPAP.
§Values are medians with 25th, 75th centiles. Data analyzed by Mann-Whitney U test.