Current Concepts

Successful Extubation of Newborn Infants Without Preextubation Trial of Continuous Positive Airway Pressure

EUN H. KIM, MD

Sixty newborn infants who had been mechanically ventilated through 3.0- or 3.5-mm endotracheal tubes were studied to examine the necessity of a preextubation trial of continuous positive airway pressure (CPAP). Thirty randomly assigned study infants were directly extubated from intermittent mandatory ventilation rates of six per minute; 30 randomly assigned control infants were extubated after a six-hour trial of continuous positive airway pressure of 3 cm H_2O. Changes in respiratory rate, in PCO_2, and in PO_2/FIO_2 were similar. All 30 study infants tolerated direct extubation without significant apnea or respiratory acidosis. Two study and eight control infants developed apnea during six hours after intermittent mandatory ventilation was discontinued ($\chi^2 = 4.3$, $P < .05$). Five control and no study infants had apneic episodes ≥ 0.5 per hour ($\chi^2 = 5.5$, $P < .02$). The results of this study suggest that newborn infants may tolerate direct extubation from low intermittent mandatory ventilation rates without a preextubation trial of CPAP. A preextubation trial of CPAP appears to be unnecessary and may cause more frequent apnea in newborn infants if used for more than several hours.

Since 1976, when Berman et al demonstrated that newborn infants maintained more functional residual capacity while on continuous positive airway pressure (CPAP) of 2 to 3 cm H_2O than on zero end expiratory pressure,[1] it has become a common practice to use CPAP for periods of up to 24 hours before attempting extubation in newborn infants after mechanical ventilation.[2-4] A preextubation trial of CPAP is recommended to insure that infants will not become exhausted without mechanical ventilation,[5,6] but no data support this recommendation. A few studies have demonstrated that airway resistance was increased through endotracheal tubes in newborn infants.[7-9] The author and a co-worker recently demonstrated that in very low birthweight infants a trial of CPAP through 2.5-mm internal diameter endotracheal tubes was associated with more apnea and mild CO_2 retention than was direct extubation from a low intermittent mandatory ventilation (IMV) rate.[10] It is the author's hypothesis that the preextubation trial of CPAP is unnecessary in newborn infants intubated with 3.0- or 3.5-mm endotracheal tubes. Therefore, this study was designed to compare the number of apneic episodes, ventilation, and oxygenation in newborns with and without a preextubation trial of CPAP.

Patients and Methods

All newborn infants who were intubated with orotracheal tubes of 3.0- or 3.5-mm internal diameter for >12 hours of mechanical

The Division of Neonatology, Department of Pediatrics, Santa Clara Valley Medical Center, San Jose, California.

Address correspondence and reprint requests to Dr. Kim, Division of Neonatology, Department of Pediatrics, Santa Clara Valley Medical Center, 751 South Bascom Avenue, San Jose, CA 95128.

0743-8346/89/ + $3.00/ + 0

ventilation were eligible for this prospective study. They were ventilated by Baby Bird (Bird Corporation, Palm Springs, Calif) or Sechrist (Sechrist Industries, Inc., Anaheim, Calif) time-cycled, pressure-limited ventilators in a conventional manner, monitored with solid-state electronic monitors. Following chest x-ray examination to confirm the position of the endotracheal tube,[6] the tubes were cut so that no more than 5 cm of the tube remained proximal to the lips. Infants with neuromuscular disorder, those who had apnea or bradycardia during the 24-hour period prior to the study, and those who were receiving CNS depressants were excluded from this study. In order to minimize the impact of apnea of prematurity on the result of this study, all infants whose corrected gestational age was <37 weeks at the time of the study were receiving theophylline either orally or intravenously to maintain serum concentration between 8 and 12 μg/mL.[4,11]

Infants were weaned from mechanical ventilators using usual clinical criteria until they reached the following preextubation settings; flow rate ≤7 L/min; peak inspiratory pressure <17 cm H_2; inspiratory time ≤0.5 seconds, positive end expiratory pressure 3 cm H_2O; and IMV rate, 6 cycles/min.

When infants were stable for at least two hours on these preextubation settings, and therefore ready for extubation as determined by the attending neonatologist, investigators assigned each infant to either the study or the control group by opening a sequentially numbered and sealed envelope containing a randomly assigned card. To assure even distribution of infants intubated with the same endotracheal tube, a separate stratum of envelopes was used for each size of the tube.

Study infants were extubated directly from the preextubation settings. Control infants received a preextubation trial of CPAP of 3 cm H_2O through endotracheal tubes for six hours.[3,4,10] All subjects were studied for the first six hours following discontinuation of mechanical ventilation (ie, six hours after extubation in the study group and six hours of CPAP through endotracheal tubes in the control group, respectively). During the six-hour observation period, a nurse was assigned at all times to each infant to monitor apnea, bradycardia, and alterations in oxygen requirement as determined by transcutaneous PO_2 monitoring to maintain PaO_2 within the range of 50 to 70 mmHg. Both respiration and heart rate were monitored by ECG-respiration monitor (Air-Shields AS-100, Air-Shields, Hatboro, Pa). Blood for gas analysis was drawn either by warmed heel stick or from a indwelling arterial catheter, but not both, at one-half, one, three, and six hours during the observation period. A chest film was taken two hours after extubation.

Apnea was defined as a cessation of spontaneous breathing for ≥20 seconds by chest wall impedence. Bradycardia was defined as a heart rate of <100 beats per minute as measured by an R-R interval ECG monitor. All bradycardia was assumed to be associated with apnea.

The following criteria were used to initiate resumption of IMV: (1) two or more episodes of severe apnea/bradycardia requiring vigorous stimulation within 30 minutes; (2) any apnea/bradycardia that would respond only to intermittent positive pressure ventilation; or (3) respiratory acidosis with a pH of <7.30.

Infants who failed extubation in one arm of the study were reventilated at levels of support that provided normal blood gas values. They were again weaned slowly to the preextubation settings. Patients were then assigned to the alternative treatment arm.

This study protocol was approved by the Research and Human Subjects Review Committee of Santa Clara Valley Medical Center. Informed consent was obtained from the parents of the infants for this study. Apnea rates (≥0.5 per hour) and success of extubated infants were compared between the two groups using chi-square analysis. In each group, the number of infants who developed apnea during the first three hours was also compared with the number during the second three hours using chi-square analysis. The changes in respiratory rate, PCO_2, and PO_2/FIO_2 during the observation period were analyzed using Student's *t* test.

Results

A total of 60 patients were enrolled in this study: 20 intubated with 3.0-mm endotracheal tubes and ten with 3.5-mm endotracheal tubes in each study and control group. Birthweight, gestational age, postnatal age, weight, PCO_2, and PO_2/FIO_2 at the time of the study were similar between the two groups (Table 1). All 30 study infants were extubated successfully. In the control group, 28 of 30 infants tolerated CPAP for six hours; the other two had to be reventilated because of significant apnea while on CPAP. Thus, the rate of success extubation was similar (30/30 vs. 28/30). The two infants who did not tolerate CPAP were later extubated successfuly directly from a low IMV rate. No infants from either group required reintubation for respiratory failure before discharge from the nursery.

During the observation period, apnea occurred in two study and eight control infants ($\chi^2 = 4.3$, $P < .05$). Five control infants and no study infants had apneic episodes ≥0.5 hour ($\chi^2 = 5.5$, $P < .02$). This is illustrated in Figure 1. Two control infants developed apnea during the first three hours, and eight during the second three hours of CPAP, a significant difference ($\chi^2 = 4.3$, $P < .05$).

There were six and four full-term infants (by corrected gestational age) in the study and control groups,

Table 1

PATIENT CHARACTERISTICS

Characteristics	ET Tubes* (mm)	Control	Study
No. of infants	3.0	20	20
	3.5	10	10
	Total	30	30
Birthweight (g);	3.0	1460 ± 480	1638 ± 515
mean ± SD	3.5	2666 ± 842	2742 ± 734
	Total	1862 ± 601	2006 ± 588
Trial weight (g);	3.0	1514 ± 368	1636 ± 448
mean ± SD	3.5	2652 ± 763	2741 ± 459
	Total	1893 ± 499	2004 ± 452
Gestational age (wk);	3.0	30.6 ± 2.7	31.7 ± 3.2
mean ± SD	3.5	36.3 ± 3.0	35.7 ± 3.7
	Total	32.5 ± 2.8	33.0 ± 3.4
Postnatal age (d);	3.0	14.8 ± 20.8	12.3 ± 18.5
mean ± SD	3.5	8.3 ± 8.4	14.6 ± 27.1
	Total	12.6 ± 16.7	13.1 ± 21.4
Pretrial PCO_2 (mmHg);	3.0	38.4 ± 6.6	38.5 ± 6.2
mean ± SD	3.5	38.9 ± 7.2	37.5 ± 8.3
	Total	38.7 ± 6.9	39.1 ± 7.8
Pretrial PO_2/FIO_2	3.0	2.6 ± 1.1	3.1 ± 1.5
(mmHg/%); mean ± SD	3.5	3.0 ± 0.8	2.7 ± 0.5
	Total	2.7 ± 1.0	3.0 ± 1.3

* ET, endotracheal.

respectively, at the time of the trial. None of the full-term infants developed apnea during the observation period. After all of the full-term infants were excluded from comparison, differences between the two groups in the number of infants with apnea and in the number of those with ≥0.5 apneic episodes per hour remained unchanged (2/24 vs. 8/26, $\chi^2 = 3.9$, $P < .05$ and 0/24 vs. 5/26, $\chi^2 = 5.1$, $P < .025$, respectively).

No significant changes were noted in postextubation chest films, respiratory rate, or PCO_2 and PO_2/FIO_2 drawn either by warmed heel stick or through indwelling arterial catheters in any group during this study (Table 2). Coincidentally, each group had 16 infants with indwelling arterial catheters: ten control and 11 study infants intubated with 3.0-mm endotracheal tubes, and six control and five study infants with 3.5-mm endotracheal tubes. Blood gas analysis drawn through the indwelling catheters confirmed the lack of difference in PCO_2 and PO_2/FIO_2 between the two groups before and during the test.

Discussion

It has been recommended and has become a common practice to use CPAP of 2 to 3 cm H_2O for up to 24 hours before attempting extubation in newborn infants after mechanical ventilation.[3-6] A preextubation trial of CPAP is used to insure that infants would not be critically exhausted without mechanical ventilation.[5] The author and a co-worker have recently demonstrated that, in very low birthweight infants intubated with 2.5-mm endotracheal tubes, a preextubation trial of CPAP is associated with more apnea and CO_2 retention when compared with direct extubation from low IMV rate.[10] We speculated that increased airway resistance through the 2.5-mm endotracheal tubes caused more frequent apnea and mild CO_2 retention during CPAP.

No data support a preextubation trial of CPAP over direct extubation in newborn infants after mechanical ventilation even through endotracheal tubes larger than 2.5 mm. LeSouef et al demonstrated that total respiratory resistance was increased when patients were intubated with 3.0- or 3.5-mm endotracheal tubes.[9] The results of this study demonstrated that a preextubation trial of CPAP through 3.0- or 3.5-mm endotracheal tubes was associated with more frequent apnea than direct extubation from low IMV rates.

The cause of apnea during CPAP through 3.0- or 3.5-mm endotracheal tubes is not known. It is speculated that increased work of breathing caused respiratory muscle fatigue which, in turn, resulted in apnea. Work

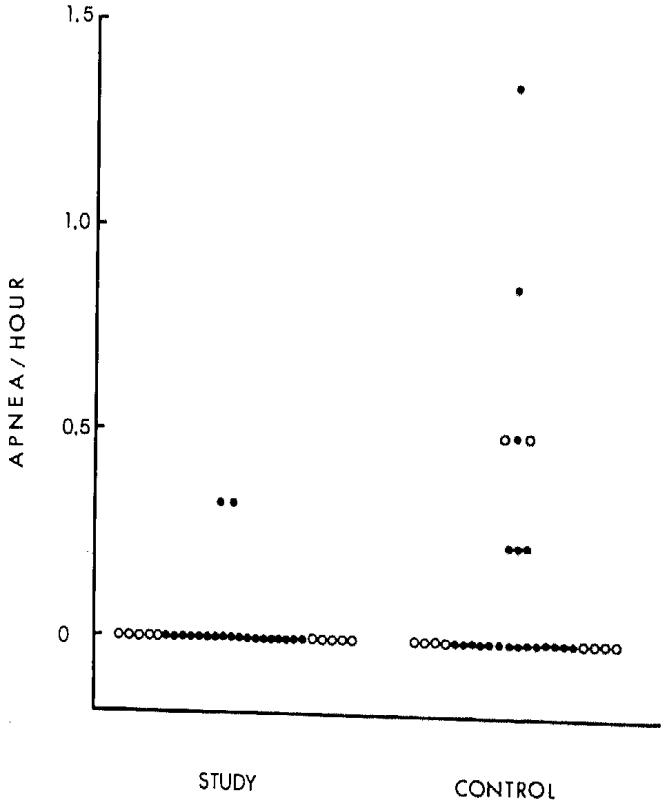

Figure 1—Frequency of apneic episodes during six hours of observation period. O, newborns intubated with 3.5-mm endotracheal tubes; ●, newborns intubated with 3.0-mm endotracheal tubes. Refer to the text for comparison between the two groups.

Table 2

*CHANGES IN PCO_2 AND PO_2/FIO_2 AFTER DISCONTINUATION OF MECHANICAL VENTILATION**

Time (hr)	Control N	Control PCO_2 (mmHg); mean ± SD	Control PO_2/FIO_2 (mmHg/%); mean ± SD	Study N	Study PO_2 (mmHg); mean ± SD	Study PO_2/FIO_2 (mmHg/%); mean ± SD
Both 3.0- and 3.5-mm ET tubes†						
Pre	30	38.7 ± 6.9	2.7 ± 1.0	30	39 ± 7.8	3.0 ± 1.3
½	25	39.6 ± 8.0	2.8 ± 1.1	22	40.8 ± 10	2.8 ± 1.8
1	24	39.5 ± 8.0	2.4 ± 0.9	26	38.7 ± 8.3	2.9 ± 1.8
3	24	39.5 ± 7.1	2.2 ± 0.6	20	38.9 ± 8.8	3.2 ± 1.6
6	26	38.5 ± 7.2	2.4 ± 0.8	27	41 ± 7	2.7 ± 1.1
3.0-mm ET tubes only						
Pre	20	38.4 ± 6.6	2.6 ± 1.1	20	38.5 ± 6.2	3.0 ± 1.3
½	20	39.2 ± 8.7	2.4 ± 1.0	15	39.5 ± 9.8	3.1 ± 1.5
1	18	39.3 ± 8.6	2.4 ± 1.0	19	39.1 ± 8.6	2.9 ± 1.5
3	17	38.1 ± 7.5	2.4 ± 0.6	17	38.8 ± 9.2	3.2 ± 1.8
6	17	37.5 ± 7.2	2.4 ± 0.9	18	38.8 ± 9.2	2.9 ± 1.3
3.5-mm ET tubes only						
Pre	10	38.9 ± 7.2	3.0 ± 0.8	10	37.5 ± 8.3	2.7 ± 0.5
½	5	41.6 ± 4.7	2.3 ± 0.7	7	43.4 ± 10.8	2.3 ± 0.8
1	6	40.5 ± 6.7	2.7 ± 0.7	7	37.7 ± 8.1	2.6 ± 0.9
3	7	43 ± 5	2.2 ± 0.8	3	39.7 ± 8.0	3 ± 0.5
6	9	41.4 ± 7.3	2.4 ± 0.6	9	44.6 ± 5.7	2.4 ± 0.7

* There was no difference in values between control and study groups in any given time, or between pretrial and trial values. This was confirmed by blood gas measurements drawn through indwelling arterial lines in 16 infants of each group.

† ET, endotracheal

of breathing was not measured in this study, but Le-Souef et al showed that 25% of the infants developed fatigue-related apnea during CPAP through endotracheal tubes.[9] As expected, no full-term infants developed apnea during the observation period in either group. However, the number of full-term infants was very small, and therefore no conclusion could be reached in this study.

Our previous study demonstrated that CPAP through 2.5-mm endotracheal tubes caused mild CO_2 retention in very low birth weight infants, further supporting previous hypotheses that CPAP through a small endotracheal tube might increase airway resistance.[7-9] This study did not show CO_2 retention in larger infants intubated with 3.0- or 3.5-mm endotracheal tubes. It is speculated that larger newborn infants were able to maintain normal PCO_2 during the six hours of the observation period by increasing their work of breathing to compensate for mildly elevated airway resistance. In this study, more neonates developed apnea during the second three hours than the first three hours of CPAP through endotracheal tubes. One may speculate that if the preextubation trial of CPAP through an endotracheal tube had been applied for 12 to 24 hours as recommended,[5] even more neonates might have developed apnea and/or CO_2 retention as a result of respiratory muscle fatigue.

In summary, a six-hour preextubation trial of CPAP was associated with more apneic episodes than direct extubation in premature infants. A prolonged preextubation trial of CPAP (ie, more than three hours) may be unnecessary and may cause more frequent apnea in preterm newborns.

Acknowledgment

Dr. Ronald S. Cohen reviewed the manuscript and provided the author with critical suggestions. The author thanks Pramela Ramachandran, MD, and Walter C. Boutwell, MD, for their cooperation in this study.

References

1. Berman LS, Fox WW, Raphaely RC, et al: Optimum levels of CPAP for tracheal extubation of newborn infants. J Pediatr 89:109, 1976
2. Fox WW, Berman LS, Dinwiddie R, et al: Tracheal extubation of the

neonate at 2-3 cm H_2O continuous positive airway pressure. Pediatrics 59:257, 1977

3. Fox WW, Schwartz JG, Shaffer TH: Successful extubation of neonates: Clinical and physiological factors. Crit Care Med 9:823, 1981
4. Barr PA: Weaning very low birth weight infants from mechanical ventilation using intermittent mandatory ventilation and theophylline. Arch Dis Child 53:598, 1978
5. Nugent J, Hanks H, Goldsmith JP: Pulmonary care. In Goldsmith JP, Karotkin EH (eds): Assisted Ventilation of the Neonate. Philadelphia, WB Saunders, 1981, pp 67-80
6. Brady JP, Gregory G: Assisted ventilation. In Klaus MH, Fanaroff AA (eds): Care of the High-Risk Neonate. Philadelphia, WB Saunders, 1986, pp 202-219
7. Cave P, Fletcher G: Resistance of nasotracheal tubes used in infants. Anesthesiology 29:588, 1968
8. Wall MA: Infant endotracheal tube resistance: Effects of changing length, diameter and gas density. Crit Care Med 8:38, 1980
9. LeSouef PN, England SJ, Bryan AC: Total resistance of the respiratory system in preterm infants with and without an endotracheal tube. J Pediatr 104:108, 1984
10. Kim EH, Boutwell WC: Successful direct extubation of very low birth weight infants from low intermittent mandatory ventilation rate. Pediatrics 80:409, 1987
11. Harris MC, Baumgart S, Rooklin AR, et al: Successful extubation of infants with respiratory distress syndrome using aminophylline. J Pediatr 103:303, 1983