Oxygen Delivery Through Nasal Cannulae to Preterm Infants: Can Practice Be Improved?

Michele Walsh, MD, MS*; William Engle, MD‡; Abbot Laptook, MD§; S. Nadya J. Kazzi, MD, MPH‖; Susie Buchter, MD¶; Maynard Rasmussen, MD#; and Qing Yao, PhD**; for the National Institute of Child Health and Human Development Neonatal Research Network

ABSTRACT. *Objective.* **Oxygen delivery through nasal cannulae to convalescent preterm infants is a common but largely unstudied practice. To learn more about current nasal cannula oxygen delivery practices, we examined the variations in oxygen delivery through nasal cannulae among the centers of the Neonatal Research Network, the frequency of prescription of low levels of oxygen, and the success of weaning to room air. We hypothesized that some infants treated with oxygen through nasal cannulae were receiving oxygen levels equivalent to those of room air.**

Methods. **This was a descriptive, nested, cohort study of nasal cannula oxygen prescription among 187 infants with birth weights of <1250 g. All infants were studied at a postmenstrual age of 36 weeks, with a timed oxygen reduction challenge to establish their ability to be weaned to room air. The results of this challenge were compared with the fraction of inspired oxygen (F_{IO_2}) delivered, calculated as effective F_{IO_2}. Infants who maintained oxygen saturation values of ≥90% during oxygen weaning and during a 30-minute period in room air were defined as passing the challenge.**

Results. **Fifty-two infants (27.8%) were receiving oxygen concentrations and flow rates through nasal cannulae that delivered an effective F_{IO_2} of <0.23, of whom 16 were receiving oxygen concentrations and flow rates that delivered an effective F_{IO_2} of 0.21. In addition, 22 infants (11.8%) were prescribed room air through nasal cannulae intentionally. Seventy-two percent of those prescribed an effective F_{IO_2} of <0.23 passed the room air challenge.**

Conclusions. **Prescription of oxygen with combinations of flow rates and oxygen concentrations that delivered a low effective F_{IO_2} was common. We speculate that some of this, including the inadvertent prescription of an effective F_{IO_2} equivalent to that of room air, is related to lack of knowledge of the effective F_{IO_2}. Routine calculation of effective F_{IO_2} values may prompt earlier trials of room air and thus reduce unnecessary days of oxygen therapy. *Pediatrics* 2005;116:857–861; *oxygen therapy, premature infants.***

From the *Case Western Reserve University, Cleveland, Ohio; ‡Indiana University, Indianapolis, Indiana; §Brown University, Providence, Rhode Island; ‖Wayne State University, Detroit, Michigan; ¶Emory University, Atlanta, Georgia; #University of California, San Diego, San Diego, California; and **Research Triangle Institute, Research Triangle Park, North Carolina.
Accepted for publication Dec 29, 2004.
doi:10.1542/peds.2004-2411
No conflict of interest declared.
Address correspondence to Michele Walsh, MD, MS, Division of Neonatology, Rainbow Babies and Children's Hospital, Case Western Reserve University, Mailstop 6010, 11100 Euclid Ave, Cleveland, OH 44106-6010. E-mail: mcw3@po.cwru.edu

ABBREVIATIONS. F_{IO_2}, fraction of inspired oxygen; STOP-ROP, Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity.

Oxygen delivery through nasal cannulae to convalescent preterm infants is a common but largely unstudied practice. There are no existing criteria regarding when personnel attempt to wean infants from oxygen or the methods of weaning used. When oxygen is delivered through a hood, the fraction of inspired oxygen (F_{IO_2}) is analyzed and often weaning increments of 2% are used. In contrast, when oxygen is delivered through a nasal cannula, the precise F_{IO_2} is unknown and weaning practices are more variable. The actual concentration of oxygen delivered through a nasal cannula is a blend of nasally inhaled oxygen and room air entrained through the mouth and nose. The ratio of these 2 components determines the actual oxygen concentration delivered to the alveoli, termed the effective F_{IO_2}. The effective F_{IO_2} varies with minute ventilation, the inspiratory oxygen concentration in ambient air and the nasal cannula, and the ratio of mouth to nose breathing.[1–3] Benaron and Benitz[1] calculated formulae predicting oxygen delivery on the basis of assumptions about patient-controlled factors. The mathematical formulae generated by Benaron and Benitz[1] were made more accessible through transformation to tabular form as a component of the Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP) trial.[4] Although these principles potentially provide a more rational basis for oxygen prescription through nasal cannulae, they have not been used widely in clinical practice. To learn more about current nasal cannula oxygen delivery practices, we examined the variations in oxygen delivery through nasal cannulae among the centers of the Neonatal Research Network, the frequency of prescription of low levels of oxygen, and the success of weaning to room air. We hypothesized that a proportion of infants treated with oxygen through nasal cannulae were receiving oxygen levels equivalent to those in room air.

METHODS

This study was nested within a randomized, controlled trial of quality improvement practices to reduce the incidence of bronchopulmonary dysplasia. Patients were eligible for the study if they had been born in a National Institute of Child Health and

Human Development Neonatal Research Center, with a birth weight of <1250 g, between May 2001 and May 2002. Within the trial, extensive data on oxygen treatment practices were collected for 1508 enrolled infants. At postmenstrual ages of 35 to 37 weeks, 209 infants were tested with a timed oxygen reduction to room air, to determine their oxygen saturation in room air. Detailed methods were reported previously.[5,6] Briefly, infants were challenged if supplemental oxygen levels were <30% at rest with oxygen saturation between 90% and 96% or were ≥30% with saturation of >96%. For infants receiving oxygen through hoods, oxygen was weaned in 2% increments. For infants receiving oxygen through nasal cannulae, flow was weaned initially in increments (for flow of 1.0–2.0 L/minute, increments of 0.5 L/minute; for flow of 0.1–0.99 L/minute, increments of 0.1 L/minute), and then oxygen concentrations were reduced to those of room air in increments of 20%. Cannulae were removed from the nares for the remainder of the challenge. There were 2 methods of passing during the room air observation phase, ie, a rapid pass and a pass after full monitoring. Rapid pass criteria were met with successful weaning to room air with all saturation values being ≥96% for 15 minutes. If the saturation values were 90% to 95%, then the infant was monitored for 30 minutes with room air; a pass was defined when all saturation values exceeded 90% in that 30-minute period.

Two hundred nine infants were challenged. Twenty-two infants were excluded from analysis because they were treated with oxygen through a hood or had incomplete information. Therefore, data for 187 (91%) of the 209 infants who were receiving oxygen supplementation through nasal cannulae were included in this study (birth weight: 843 ± 186 g, mean ± SD; gestational age: 26.3 ± 1.8 weeks; weight at time of study: 2014 ± 369 g).

For all neonates who were receiving oxygen through nasal cannulae, effective FIO_2 values were calculated with the equations described by Benaron and Benitz,[1] as modified by the STOP-ROP study investigators[4] (Tables 1 and 2). A hypothetical neonate weighing 2.0 kg with nasal cannula flow of 0.03 L/minute and 30% oxygen concentration is used to illustrate the use of Tables 1 and 2. In Table 1, weight and flow are compared and yield a factor of 2. In Table 2, the factor of 2 is combined with the oxygen concentration of 30% to yield a predicted effective FIO_2 of 0.21. In their calculations, Benaron and Benitz[1] assumed the following constant variables: nasal flow is constant over the inspiratory cycle, the upper airway does not serve as a reservoir, the inspiration time is 0.3 seconds, and the tidal volume is 5.0 mL/kg. To assess the value of knowing the effective FIO_2, the outcome of the room air challenge was compared with the effective FIO_2 received before the challenge.

The institutional review boards at the 17 participating centers approved the physiologic definition of bronchopulmonary dysplasia protocol. Parental consent was obtained as required by local institutional review board policies. Continuous variables are described as mean and SD. Group differences in continuous measures were compared with Student's t test and analysis of variance. Categorical variables were assessed with frequency distributions, and group differences were compared with the χ^2 test. To determine the ability of the effective FIO_2 to predict the success of weaning to room air, logistic regression equations were constructed. Candidate predictor variables included gender, birth weight, gestational age, weight at the time of study, saturation before challenge, and effective FIO_2. Various effective FIO_2 levels and combinations of prechallenge effective FIO_2 and saturation were assessed for their ability to predict successful passing of the challenge.

RESULTS

Centers differed in their methods of delivering oxygen through nasal cannulae, with 3 centers using 100% oxygen with various flow rates and 14 centers using blended oxygen with various flow rates. Of the 187 neonates who were receiving oxygen through nasal cannulae, 87 (46.5%) passed the room air challenge and 100 (53.5%) failed. The effective FIO_2 delivered before the challenge ranged from 0.21 to 0.49. As expected, the frequency of success varied, with infants treated with lower effective FIO_2 levels being more successful in passing the challenge (Fig 1). The effective FIO_2 for those who passed was 0.23 ± 0.03 (mean ± SD), compared with 0.26 ± 0.05 for those who failed. The success of weaning was associated with the effective FIO_2 before the challenge ($P < .0001$) (Fig 1).

Prescription of oxygen with combinations of flow rates and oxygen concentrations that produced low effective FIO_2 values was common. Fifty-two infants (27.8%) were receiving oxygen concentrations and flow rates through nasal cannulae that delivered an effective FIO_2 of <0.23; 16 infants (8.6%) were receiving oxygen concentrations and flow rates that delivered an effective FIO_2 of 0.21 and thus were being prescribed room air. In contrast, among those prescribed oxygen through a hood, none was prescribed <23% oxygen.

Twenty-two infants (11.8%) were prescribed room air through nasal cannulae intentionally, with various flow rates (range: 0.13–2.00 L/minute). Fifteen (68.2%) of those 22 infants passed the challenge successfully, whereas 7 failed.

Logistic regression analysis identified effective FIO_2 and oxygen saturation before the weaning challenge as significant factors associated with successful weaning to room air (Table 3). Gestational age and birth weight were not predictors of successful wean-

TABLE 1. Calculation of Effective FIO_2, Step 1

Flow, L/min	Factor With Weight of								
	0.7 kg	1.0 kg	1.25 kg	1.5 kg	2 kg	2.5 kg	3 kg	3.5 kg	4 kg
0.01	1	1	1	1	1	0	0	0	0
0.03 (1/32)	4	3	2	2	2	1	1	1	1
0.06 (1/16)	9	6	5	4	3	2	2	2	2
0.125 (1/8)	18	12	10	8	6	4	4	4	4
0.15	21	15	12	10	8	6	5	4	4
0.25 (1/4)	36	25	20	17	13	10	8	7	6
0.5 (1/2)	71	50	40	33	25	20	17	14	13
0.75 (3/4)	100	75	60	50	38	30	25	21	19
1.0 (1.0)	100	100	80	67	50	40	33	29	25
1.25	100	100	100	83	63	50	42	36	31
1.5	100	100	100	100	75	60	50	43	38
2.0	100	100	100	100	100	80	67	57	50
3.0	100	100	100	100	100	100	100	86	75

Adapted from equations 3 and 4 in ref 1. The rule of thumb (implicit in the table) is that, for most infants in the STOP-ROP study, if flow (in liters per minute) exceeds body weight (in kilograms), then the effective FIO_2 equals the nasal cannula oxygen concentration.

TABLE 2. Calculation of Effective FIO_2, Step 2

Factor	Effective FIO_2 With Oxygen Concentration of						
	0.21	0.22	0.25	0.30	0.40	0.50	1.00
0	0.21	0.21	0.21	0.21	0.21	0.21	0.21
1	0.21	0.21	0.21	0.21	0.21	0.21	0.22
2	0.21	0.21	0.21	0.21	0.21	0.22	0.23
3	0.21	0.21	0.21	0.21	0.22	0.22	0.23
4	0.21	0.21	0.21	0.21	0.22	0.22	0.24
5	0.21	0.21	0.21	0.21	0.22	0.22	0.25
6	0.21	0.21	0.21	0.22	0.22	0.23	0.26
7	0.21	0.21	0.21	0.22	0.22	0.23	0.27
8	0.21	0.21	0.21	0.22	0.23	0.23	0.27
9	0.21	0.21	0.21	0.22	0.23	0.24	0.28
10	0.21	0.21	0.21	0.22	0.23	0.24	0.29
11	0.21	0.21	0.21	0.22	0.23	0.24	0.30
12	0.21	0.21	0.21	0.22	0.23	0.24	0.30
13	0.21	0.21	0.22	0.22	0.23	0.25	0.31
14	0.21	0.21	0.22	0.22	0.24	0.25	0.32
15	0.21	0.21	0.22	0.22	0.23	0.25	0.33
17	0.21	0.21	0.22	0.23	0.24	0.26	0.34
18	0.21	0.21	0.22	0.23	0.24	0.26	0.35
19	0.21	0.21	0.22	0.23	0.25	0.27	0.36
20	0.21	0.21	0.22	0.23	0.25	0.27	0.37
21	0.21	0.21	0.22	0.23	0.25	0.27	0.38
22	0.21	0.21	0.22	0.23	0.25	0.27	0.36
23	0.21	0.21	0.22	0.23	0.25	0.28	0.39
25	0.21	0.21	0.22	0.23	0.25	0.28	0.41
27	0.21	0.21	0.22	0.23	0.25	0.29	0.42
28	0.21	0.21	0.22	0.24	0.26	0.29	0.43
29	0.21	0.21	0.22	0.24	0.27	0.29	0.44
30	0.21	0.21	0.22	0.24	0.27	0.30	0.45
31	0.21	0.21	0.22	0.24	0.27	0.31	0.47
33	0.21	0.21	0.22	0.24	0.27	0.31	0.47
36	0.21	0.21	0.22	0.24	0.28	0.31	0.49
38	0.21	0.21	0.23	0.24	0.28	0.32	0.51
40	0.21	0.21	0.23	0.25	0.29	0.33	0.53
42	0.21	0.21	0.23	0.25	0.29	0.33	0.54
43	0.21	0.21	0.23	0.25	0.29	0.33	0.55
44	0.21	0.21	0.23	0.25	0.29	0.34	0.56
50	0.21	0.21	0.23	0.25	0.30	0.35	0.60
55	0.21	0.22	0.23	0.26	0.31	0.37	0.64
57	0.21	0.22	0.23	0.26	0.32	0.38	0.66
60	0.21	0.22	0.23	0.26	0.32	0.38	0.68
63	0.21	0.22	0.24	0.27	0.33	0.39	0.71
67	0.21	0.22	0.24	0.27	0.34	0.40	0.74
71	0.21	0.22	0.24	0.27	0.34	0.42	0.77
75	0.21	0.22	0.24	0.28	0.35	0.43	0.80
80	0.21	0.22	0.24	0.28	0.36	0.44	0.84
83	0.21	0.22	0.24	0.28	0.37	0.45	0.87
86	0.21	0.22	0.24	0.29	0.37	0.46	0.89
100	0.21	0.22	0.25	0.30	0.40	0.50	1.00

Adapted from equations 3 and 4 in reference 1.

ing. The combination of prechallenge saturation of >96% and effective FIO_2 of ≤0.23 identified correctly 66.3% of infants who were weaned successfully to room air (Table 4).

DISCUSSION

Oxygen is delivered nearly exclusively through nasal cannulae for preterm infants at the postmenstrual age of 36 weeks. Fifty-two (27.8%) of the infants prescribed oxygen through nasal cannulae in this study were prescribed amounts of <23%, which would not be prescribed routinely if the same infants were in oxygen hoods. Furthermore, 72% of the infants prescribed <23% oxygen were weaned successfully to room air when challenged. The combination of prechallenge saturation of >96% and effective FIO_2 of ≤0.23 correctly identified 66.3% of infants who were weaned successfully to room air. Therefore, knowledge of the effective FIO_2 delivered through nasal cannulae may allow caretakers to identify more effectively infants who are ready for a trial of room air. Widespread clinical use of the effective FIO_2 for infants treated with nasal cannulae may make their treatment more similar to that of infants treated with oxygen in hoods.

Oxygen delivery through nasal cannulae for neonates is preferred by caregivers because of the ease of administration and the ability to feed and to care for the infant while continuing oxygen administration. Infants cared for with nasal cannulae also have increased mobility, compared with those who are in hoods, which may increase interactions with the parents, caregivers, and environment and may be developmentally beneficial. These benefits are balanced by some drawbacks, including the instability of oxygen administration in transitions between oral and nasal

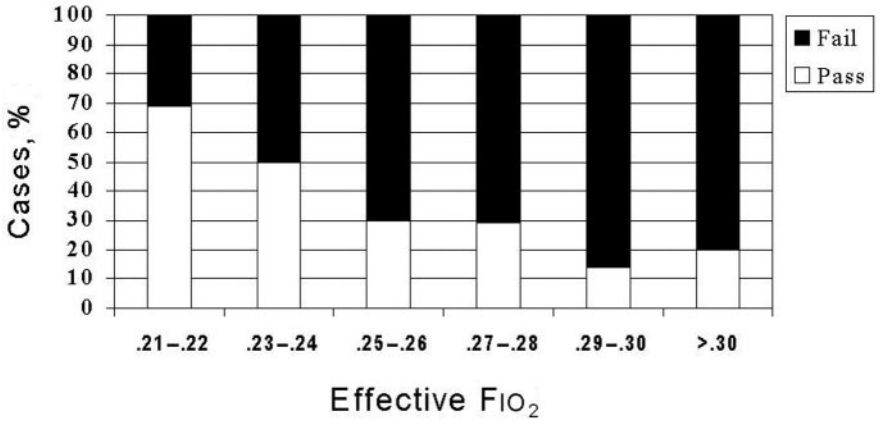

Fig 1. Outcomes of room air challenge compared with effective F_{IO_2} values.

TABLE 3. Predictors of Successful Weaning to Room Air

Parameter	Odds Ratio Point Estimate	95% Confidence Interval
Gender (female vs male)	0.967	0.479–1.954
Multiple birth (yes vs no)	0.644	0.308–1.346
Gestational age	1.030	0.854–1.242
Weight	1.000	0.999–1.001
Average saturation	1.303	1.134–1.497
Effective F_{IO_2} of 0.21 (yes vs no)	4.192	1.731–10.155

breathing, drying of nasal mucosa, and lack of precise knowledge about the delivered oxygen concentration. The last factor may contribute to highly variable weaning practices among institutions and physicians and to continued prescription of oxygen through nasal cannulae that delivers concentrations of oxygen that are effectively room air. Such practices might contribute to unnecessary days of oxygen delivery, hospitalization, and costs of care.

Few studies have explored the delivery of oxygen through nasal cannulae to convalescent preterm infants since its use was proposed in the 1980s.[7] Fan and Voyles[8] proposed a method for estimating the concentration of delivered oxygen by matching pulse oximetry measurements in a nasal cannula with similar saturation values in an oxygen hood. Benaron and Benitz[1] proposed the technique used here in 1994, whereas Finer et al[9] proposed a similar method in 1996. Despite these recommendations, routine documentation of the estimated effective F_{IO_2} delivered through nasal cannulae has not been implemented in clinical practice. We speculate that in part this is because the methods of both Benaron and Benitz[1] and Finer et al[9] require calculations that are cumbersome during routine clinical care. Tables that display this information make the information more accessible and may improve nasal cannula oxygen prescription.

The use of nasal cannulae to deliver end-expiratory pressure or gas flow to reduce the frequency of apnea and desaturation has not been tested adequately, although such use has become common. Several studies have documented that nasal cannulae can deliver positive end-expiratory pressure. Locke et al[10] first described the ability of nasal cannulae to generate inadvertent positive end-distending pressure. Others later exploited this possibility as a deliberate therapeutic intervention. Courtney et al[11] documented that continuous positive airway pressure delivered through nasal cannulae led to changes in lung volume but did so at the cost of increased work of breathing and higher oxygen concentrations. Sreenan et al[12] found that nasal cannulae used at flow rates between 1.0 and 2.5 L/minute for preterm infants delivered continuous positive airway pressures as high as 8 cm H_2O and performed equivalently to conventional continuous positive airway pressure delivery among infants who were studied at a mean weight of 1260 g. Of interest, 22 infants in the present study were treated with nasal cannulae with room air and flow rates ranging from 0.13 to 2.00 L/minute. Fifteen (68.2%) of those infants were weaned successfully to room air, but 31.8% were not. It is possible that the flow for the patients who experienced failure stabilized the airway through the administration of continuous positive airway pressure.

Our study has limitations that must be recognized. One limitation is the relatively brief period for the trial in room air (30 minutes).[5, 6] The room air challenge was designed to define bronchopulmonary dysplasia as a clinical trial end point. All infants were returned to their preexisting oxygen concentrations. Therefore, the results of the room air trial may not translate into the ability to tolerate prolonged weaning to room air. Nevertheless, the identification of a possible lower weaning limit for nasal cannula therapy may be an important step in improving oxygen-weaning practices. Clinicians using this strategy should implement a longer period of observation, including sustained monitoring in room air, to ensure that short periods of adequate oxygen saturation translate to longer-term oxygenation and cardiopulmonary stability before discharge. A second limitation is that the calculation of effective F_{IO_2} necessarily makes assumptions about inspiratory time and tidal volume. These assumptions may not apply for specific infants, which might account for some of the infants who experienced failure but were predicted to pass. Finally, numerous vendors produce nasal cannulae with different widths. The impact of differences between devices is not known.

The calculation of effective F_{IO_2} is a step toward

TABLE 4. Performance of Different Cutoff Parameters for Predicting Success of Weaning to Room Air

Cutoff	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
F_{IO_2} of ≤0.23	76.19	55.29	54.63	76.67
F_{IO_2} of ≤0.24	79.59	47.6	51.77	76.74
F_{IO_2} of ≤0.25	87.76	35.1	48.86	80.22
Saturation of >96%	66.22	55.77	51.58	69.88
F_{IO_2} of ≤0.23 and saturation of >96%	45.89	83.57	66.34	68.65
F_{IO_2} of ≤0.24 and saturation of >96%	48.63	80.19	63.39	68.88
F_{IO_2} of ≤0.25 and saturation of >96%	54.11	75.85	61.24	70.09

more rational prescription of oxygen through nasal cannulae for convalescent preterm neonates. Identification of the point at which the effective F_{IO_2} reaches 0.23 allows clinicians to identify a point at which it is logical to perform a trial of room air. Not all infants will pass the trial, but such an attempt may reduce unnecessary days with low levels of oxygen and may reduce the length of the hospital stay.

ACKNOWLEDGMENTS

This work was supported by the National Institute of Child Health and Human Development (grants U10-HD34216, U10-HD21364, U10-HD27853, U10-HD27851, U01-HD36790, U10-HD27856, U10-HD21397, U10-HD27881, U10-HD27880, U10-HD21415, U10-HD21373, U10-HD21385, U10-HD27871, U10-HD34167, and U10-HD27904) and the General Clinical Research Center (grants M01-RR08084, M01-RR00750, M01-RR00997, M01-RR00070, M01-RR06022, M01-RR02635, M01-RR02172, and M01-RR01032).

Additional participants were as follows: Advisory Committee: M. C. Walsh, MD, MS, and A. A. Fanaroff, MD, Case Western Reserve University (Cleveland, OH); A. H. Jobe, MD, PhD, University of Cincinnati (Cincinnati, OH); R. Higgins, MD, National Institute of Child Health and Human Development (Bethesda, MD); N. Finer, MD, University of California, San Diego (San Diego, CA); K. Poole, PhD, Research Triangle Institute (Research Triangle Park, NC); Intervention Centers: S. Nadya Kazzi, MD, MPH, K. Hayes-Hart, RN, M. Betts, RRT, S. Shankaran, MD, principal investigator, and G. Muran, RN, Wayne State University (Detroit, MI); A. Laptook, MD, M. Martin, RN, and J. Allen, RRT, University of Texas Southwestern (Dallas, TX); W. A. Engle, MD, L. Miller, RN, R. Hooper, RRT, and J. Lemons, MD, principal investigator, Indiana University (Indianapolis, IN); W. Rhine, MD, C. Kibler, RN, J. Parker, RRT, D. Stevenson, MD, principal investigator, and B. Ball, BS, Stanford University (Palo Alto, CA); M. Rasmussen, MD, M. Grabarczyk, BSN, C. Joseph, RRT, and K. Arnell, BSN, Sharp Mary Birch Hospital for Women (San Diego, CA); G. Heldt, MD, R. Bridge, RN, J. Goodmar, RRT, N. Finer, MD, and C. Henderson, RCP, University of California, San Diego (San Diego, CA); S. Buchter, MD, M. Berry, RN, I. Seabrook, RRT, B. Stoll, MD, principal investigator, and E. Hale, RN, Emory University (Atlanta, GA); Benchmark Centers: S. Duara, MD, and R. Everette, RN, University of Miami (Miami, FL); W. Carlo, MD, and M. Collins, RN, University of Alabama (Birmingham, AL); W. Oh, MD, and A. Hensman, RN, Brown University (Providence, RI); Control Centers: M. T. O'Shea, MD, MPH, and N. Peters, RN, Wake Forest University (Winston-Salem, NC); J. Tyson, MD, MPH, and G. McDavid, RN, University of Texas (Houston, TX); A. A. Fanaroff, MD, M. C. Walsh, MD, MS, and N. Newman, RN, Case Western Reserve University (Cleveland, OH); D. Phelps, MD, and L. Reubens, RN, University of Rochester (Rochester, NY); R. A. Ehrenkranz, MD, and P. Gettner, RN, Yale University (New Haven, CT); C. Michael Cotton, MD, and K. Auten, RN, Duke University (Durham, NC); E. Donovan, MD, and C. Grisby, RN, University of Cincinnati (Cincinnati, OH); Statistical Center: Qing Yao, PhD, and Ken Poole, PhD, Research Triangle Institute (Research Triangle Park, NC).

We thank the infants and their families who participated in the study. We also acknowledge the pioneering work of David Benaron and William Benitz, who developed originally the effective F_{IO_2} concept, without which this work could not have been undertaken. We also thank the investigators from the STOP-ROP study for allowing us to use the effective F_{IO_2} tables; their work was supported by the National Eye Institute (grant EY09962).

REFERENCES

1. Benaron DA, Benitz WE. Maximizing the stability of oxygen delivered via nasal cannula. *Arch Pediatr Adolesc Med.* 1994;148:294–300
2. Miller MJ, Martin RJ, Carlo WA, et al. Oral breathing in newborn infants. *J Pediatr.* 1985;107:465–469
3. Miller MJ, Carlo WA, Strohl KP, Fanaroff AA, Martin RJ. Effect of maturation on oral breathing in sleeping premature infants. *J Pediatr.* 1986;109:515–519
4. Phelps DL, STOP-ROP Multicenter Study Group. Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP), a randomized, controlled trial, I: primary outcomes. *Pediatrics.* 2000;105:295–310
5. Walsh MC, Wilson-Costello D, Zadell A, Newman N, Fanaroff AA. Safety, reliability and validity of a physiologic definition of bronchopulmonary dysplasia. *J Perinatol.* 2003;23:451–456
6. Walsh MC, Yao Q, Gettner P, et al. Impact of a physiologic definition on bronchopulmonary dysplasia rates. *Pediatrics.* 2004;114:1305–1311
7. Kloor TH Jr, Carbajal D. Infant oxygen administration by modified nasal cannula. *Clin Pediatr (Phila).* 1984;23:447–449
8. Fan LL, Voyles JB. Determination of inspired oxygen delivered by nasal cannula in infants with chronic lung disease. *J Pediatr.* 1983;103:923–925
9. Finer NN, Bates R, Tomat P. Low flow oxygen delivery via nasal cannula to neonates. *Pediatr Pulmonol.* 1996;21:48–51
10. Locke RG, Wolfson MR, Shaffer TH, Rubenstein SD, Greenspan JS. Inadvertent administration of positive end-distending pressure during nasal cannula flow. *Pediatrics.* 1993;91:135–138
11. Courtney SE, Pyon KH, Saslow JG, Aronold GK, Pandit PB, Habib RH. Lung recruitment and breathing pattern during variable versus continuous flow nasal continuous positive airway pressure in premature infants: an evaluation of three devices. *Pediatrics.* 2001;107:304–308
12. Sreenan C, Lemke RP, Hudson-Mason A, Osivich H. High-flow nasal cannulae in the management of apnea of prematurity: a comparison with conventional nasal continuous positive airway pressure. *Pediatrics.* 2002;109:1081–1083