Published in final edited form as:

Pediatr Pulmonol. 2016 November ; 51(11): 1206–1211. doi:10.1002/ppul.23442.

Oxygen Weaning After Hospital Discharge in Children With Bronchopulmonary Dysplasia

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Summary

Background—In the United States, approximately 12,000 preterm infants are diagnosed with bronchopulmonary dysplasia (BPD) and many of these infants require supplemental oxygen after initial hospital discharge. In children with BPD we sought to identify factors associated with supplemental oxygen use after initial hospital discharge, factors associated with duration of supplemental oxygen use, and methods used to wean off supplemental oxygen in the home environment.

Methods—All subjects (n = 420) with the diagnosis of BPD were recruited from a single center Bronchopulmonary Dysplasia Clinic between 2008 and 2013. Subject information was obtained from patient history records, patient demographics, and caregiver questionnaires.

Results—Younger gestational age and having a Nissen fundoplication were associated with home supplemental oxygen use in subjects with BPD. Of the 154 subjects who received supplemental oxygen at home, 38% received flows $\leq 1/8$ LPM, 30% received flows $>1/8$ LPM and $\leq 1/4$ LPM, 21% received flows $>1/4$ LPM and $\leq 1/2$ LPM, and 11% received flows $>1/2$ LPM. Among subjects receiving $\leq 1/8$ LPM of oxygen, the median age of weaning off oxygen was 10.1 months, but increased depending on level of oxygen flow at initial outpatient visit. Of the 137 subjects weaned off of oxygen during the study period, weaning was not supervised by a physician in 32.1% of subjects.

Conclusion—Home supplemental oxygen use is common in infants diagnosed with BPD. In this study, the median age of weaning off supplemental oxygen was 10.1 months after initial hospital discharge. Unsupervised weaning of supplemental oxygen occurred in 32.1% of subjects with BPD.

Keywords

Bronchopulmonary dysplasia; oxygen; prematurity; respiratory outcomes

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Conflict of interest: None.

INTRODUCTION

Very low birth weight (VLBW) infants are at highest risk for the development of bronchopulmonary dysplasia (BPD). Indeed up to 50% of preterm infants weighing less than 1,000 g will go on to develop BPD.^{1,2} In the United States, there has been a modest decline in the rate of preterm birth between 2006 and 2013, nevertheless over 50,000 preterm infants in 2013 weighed less than 1,500 g at birth. Each year approximately 12,000 preterm infants are diagnosed with BPD, making BPD one of the most common chronic pediatric respiratory diseases during infancy.³

BPD is characterized by impaired alveolar development with older children frequently exhibiting small airway dysfunction with pulmonary function tests. In addition to very low birth weight, other risk factors for BPD include intrauterine growth restriction, exposure to supplemental oxygen and/or positive pressure ventilation, pre- and postnatal infections, poor nutrition, and aspiration.⁴ Many infants diagnosed with moderate to severe BPD in the neonatal intensive care unit (NICU) are discharged home on supplemental oxygen.⁵ Currently, there are no widely accepted guidelines for weaning children off supplemental oxygen once they are discharged from the NICU. Indeed in a recent survey of pediatric pulmonologists, only 8% used a standardized protocol for weaning and a variety of measures were used to gauge readiness to wean.⁶

There have been several studies (population n ranging 20–93) examining supplemental oxygen use at home in preterm infants with a median age of weaning off of oxygen ranging from 5.5 to 8.0 months,^{7–10} but the predictors of when infants are able to be weaned off of oxygen remain poorly understood. A better understanding of factors that predict timing of oxygen weaning may help determine optimal weaning strategies for healthcare providers and provide prognostic information for caregivers, thus reducing unnecessary health care costs and burden to patient families.

To this end we hypothesized that in infants with BPD, lower birth weight and earlier gestational age would correlate with a need for supplemental oxygen at the initial outpatient pulmonary clinic visit. Furthermore, we hypothesized that children with BPD who were technology dependent (ventilator and/or feeding tube use) or who required higher liter flows of oxygen at their initial outpatient visit would wean off supplemental oxygen at a later age compared to those who were not. We also sought to determine how subjects were being weaned off supplemental oxygen after initial hospital discharge.

METHODS

Study Population

Subjects (n = 420) in this study were recruited from the outpatient Johns Hopkins Bronchopulmonary Dysplasia Clinic between January 2008 and April 2013. Local neonatologists and pediatricians refer preterm infants with respiratory disease to the clinic for follow up care, which is staffed by two board-certified pediatric pulmonologists. Inclusion criteria are being born preterm (< 36 weeks gestation), diagnosed with BPD by a pediatric pulmonologist or neonatologist per NICHD criteria (those who were on oxygen

meet criteria for moderate or severe BPD),⁵ and a minimum of 2 years of follow-up after initial pulmonary evaluation (through April 2015). This study was approved by the Johns Hopkins University Institutional Review Board (Protocol #: NA_051884) with informed consent from parents/guardians.

Demographics

Type of insurance was established using billing records. Median household income was derived from 2010 U.S. census tract data using residential zip codes (U.S. median household income: \$50,502; State of Maryland median household income: \$70,004). Race/ethnicity, primary caregiver education level, and smoking in the home environment were self-reported. If the caregiver did not complete the questionnaire on smoking, exposure was determined through chart review. The presence of gastrostomy tubes, history of Nissen fundoplication, home ventilator use, inhaled corticosteroid use before 2 years of age, pulmonary hypertension, initial discharge date, and date of first BPD clinic visit were ascertained through chart review. Indications for gastrostomy tube placement and/or Nissen fundoplications were determined by the referring NICU. Pulmonary hypertension was defined by the presence of pulmonary hypertension (pulmonary pressures $\geq 1/2$ systemic pressures) after 2 months of age by echocardiogram.¹¹

Oxygen Use and Weaning

Supplemental oxygen use was determined from clinic records. Oxygen flow was defined as the amount of home oxygen prescribed at initial discharge from the neonatal intensive care unit and was obtained through chart review; for analysis flows were arbitrarily divided in commonly used flows, $1/8$ LPM, between $>1/8$ LPM and $1/4$ LPM, between $>1/4$ LPM and $1/2$ LPM, and $>1/2$ LPM. The timing and method of oxygen weaning were determined through chart review. The date of weaning was the date of the decision to wean by a medical provider, the date of the sleep study if one was performed, or the date given by the caregiver if oxygen was discontinued by the caregiver. Duration of home oxygen use was defined as the time between initial discharge from the NICU and date of weaning. Supervised weaning was defined as weaning directed by a medical provider (in clinic, inpatient, by sleep study, or directions for how to wean at home). Subjects who underwent weaning under the supervision of the BPD clinic were assessed on extended pulse-oximetry in clinic while awake with subsequent weaning during sleep assessed through home pulse-oximetry or overnight polysomnography at the discretion of the staffing pulmonologist. Unsupervised weaning was noted when a subject on oxygen returned to clinic without oxygen and the caregiver reported stopping oxygen use.

Statistical Methods

Chi-square and *t* tests were used to compare demographic features and baseline health status indicators stratified by absence/presence of supplemental oxygen use, timing of weaning, and method of weaning. Kaplan-Meier curves were used to analyze the age of weaning among patients on home supplemental oxygen (*n* = 154). Multivariable Cox and logistic regressions were used to assess the relationship of demographic and clinical variables with presence/absence of oxygen use, timing of oxygen weaning, and supervised/unsupervised weaning. Statistically significant variables from chi-square and *t* tests were used to build

stepwise multivariate regression models. STATA IC 11 (StataCorp LP, College Station, TX) was used for analyses. *P* values <0.05 were considered statistically significant.

RESULTS

Demographics

A total of 420 subjects were recruited from the Johns Hopkins Bronchopulmonary Dysplasia Clinic, of whom 154 received supplemental oxygen at home after their initial NICU discharge (Table 1). Of these 154 subjects, 58 (38%) received flows $\leq 1/8$ LPM, 46 (30%) received flows $> 1/8$ LPM and $\leq 1/4$ LPM, 33 (21%) received flows $> 1/4$ LPM and $\leq 1/2$ LPM, and 17 (11%) received flows $> 1/2$ LPM. Five subjects (3.3%) received supplemental oxygen through a home ventilator. Infants with BPD who received oxygen were born at earlier gestational ages (26.1 vs. 27.3 weeks; $P < 0.001$), had lower birth weights (836 vs. 1,018 g; $P < 0.001$), and were discharged from the NICU at older ages (4.9 vs. 3.6 months; $P < 0.001$) compared to infants with BPD not on oxygen. Additionally, infants on oxygen were more likely to have a gastrostomy tube (34.4% vs. 17.7%; $P < 0.001$) and Nissen fundoplication (25.3% vs. 10.9%; $P < 0.001$), and be on inhaled corticosteroids during the first two years of life (85.1% vs. 74.8%; $P = 0.014$) compared to infants not on oxygen. Using multivariate regression modeling, we found that younger gestational age (adjusted OR: 0.83 per week; $P < 0.001$) and having a Nissen fundoplication (adjusted OR: 3.02; $P < 0.001$) were associated with home supplemental oxygen use. Sex, race/ethnicity, smoking in the home, and other socioeconomic characteristics did not differ between subjects receiving oxygen at home and subjects that did not.

Supplemental Oxygen and Pulmonary Hypertension

A total of 37 subjects receiving supplemental oxygen (24%) were diagnosed with pulmonary hypertension, which included 9 subjects receiving flows $\leq 1/8$ LPM, 7 subjects receiving between $> 1/8$ LPM and $\leq 1/4$ LPM, 13 subjects receiving between $> 1/4$ LPM and $\leq 1/2$ LPM, and 8 subjects receiving $> 1/2$ LPM. The amount of oxygen flow was associated with the likelihood of having a diagnosis of pulmonary hypertension ($\chi^2 P < 0.004$). Among subjects receiving $\leq 1/4$ LPM of oxygen, the prevalence of pulmonary hypertension was 15%, but rose to 39% among those receiving flows $> 1/4$ LPM and $\leq 1/2$ LPM and 47% among receiving flows $> 1/2$ LPM.

Age of Oxygen Weaning

Of the 154 subjects on supplemental oxygen, 137 (89%) were weaned off oxygen during the study period, 8 (5%) remained on oxygen, and 9 (6%) were lost to follow-up. Lost to follow-up was defined as still on oxygen with no contact within the final 12 months of the study period. The median age of weaning for the entire sample was 12.5 months (95% C.I.: 10.9, 14.2), although the median age did vary by the amount of oxygen flow at the time of NICU discharge (Fig. 1: log rank $P < 0.001$). Among subjects receiving $\leq 1/8$ LPM of oxygen, the median age of weaning was 10.1 months, but rose to 13.3 months among those receiving flows $> 1/8$ LPM and $\leq 1/2$ LPM and 33.1 months among receiving flows $> 1/2$ LPM. The mean duration of oxygen use at home for subjects weaned off during the study period was 10.9 ± 12.7 months ($n = 137$).

Children weaned after 1 year of age or still on oxygen tended to be older at the time of discharge from the NICU be older and heavier at first presentation at BPD clinic, more likely to have gastrostomy tubes, Nissen funduplications, and/or home ventilators, be prescribed inhaled corticosteroids, be diagnosed with pulmonary hypertension, and be on higher flows of oxygen at home compared to children weaned off of oxygen prior to 12 months of age (Table 2). Demographic factors, including gestational age, and socioeconomic factors were not associated with the age of oxygen weaning. Using a stepwise approach in multivariate Cox regression with factors associated with age of oxygen weaning as above, the only factors that remained associated with a later age of oxygen weaning were a later age at the time of first BPD clinic visit ($P < 0.001$), presence of a gastrostomy tube ($P = 0.001$), and inhaled corticosteroid use prior to 2 years of age ($P = 0.003$).

Oxygen Weaning Method

Of the 137 subjects weaned off of oxygen during the study period, weaning was not supervised by a physician in 32.2% of subjects (Fig. 2). The most common methods of supervised weaning were overnight polysomnography studies (45.3%) and evaluation in BPD clinic during a regular appointment (11.7%). An additional 4.4% of subjects were weaned in an inpatient setting during an admission for other medical reasons, another 4.4% were weaned at home under a pulmonologist's direction, and the last 2.3% were weaned at home under the direction of an otolaryngologist or general pediatrician. Subjects who weaned off of oxygen without physician supervision tended to be nonwhite, have a diagnosis of pulmonary hypertension, and have public insurance (Table 3). Using multivariate logistic regression modeling, we found that only a diagnosis of pulmonary hypertension (OR = 2.61, $P = 0.024$) and public insurance (OR = 2.46, $P = 0.029$) were associated with an increased risk for unsupervised weaning. The amount of oxygen flow and timing of the weaning were not associated with weaning method.

DISCUSSION

In our clinic population, we found that over one third of the preterm infants with BPD were discharged from the hospital with supplemental oxygen. These infants were more likely to have been delivered at a younger gestational age, and to have needed a Nissen fundoplication. These factors are consistent with poorer baseline health status due to greater prematurity. The median age of weaning was 12.5 months, which is longer than other previously published studies (5.5–8.0 months),^{7–10} and suggests that our study population of preterm infants may have more severe lung disease as a whole. Later weaning of oxygen was associated with use of inhaled corticosteroids, needing a gastrostomy tube, and an older age at first visit to the BPD clinic. The latter likely reflects older age at discharge with longer hospitalization due to greater prematurity.

In our patient population of children with BPD after initial hospital discharge, weaning of home oxygen was supervised in 67.9% of subjects. Most commonly safety for weaning was assessed using overnight polysomnography, which allowed quantification and qualification of oxygen desaturations during sleep. Interestingly, weaning was not supervised by a medical provider in 32.1% of subjects. Most frequently these children presented to the

medical system after caregivers had stopped administering home oxygen without medical guidance. This method of weaning is concerning since evidence exist that inadequate oxygenation may impair brain development and somatic growth^{12,13} as well alter cardiac function.^{14,15} This is a particular concern in children with BPD since they are already at increased risk of cognitive and behavioral abnormalities and pulmonary hypertension due to poor lung growth.

Unsupervised oxygen weaning and a concomitant diagnosis of pulmonary hypertension in BPD infants is of particular concern due to high mortality rates of 14–38%.¹⁶ These infants are in even greater need of appropriate supplemental oxygenation with close supervision by a physician, particularly during weaning. It is unclear from our study why families discontinue use of supplemental oxygen prematurely and will need to be addressed in future studies.

This study's strengths include a substantial population of preterm infants diagnosed with BPD before hospital discharge and the capacity to follow these infants longitudinally in a BPD disease specific clinic. Limitations include that this study was performed at a single center's outpatient clinic and may not necessarily be generalizable. Other limitations include the primarily urban population served by the institution and its role as a tertiary care center, which may increase the number of severe cases that were referred to the BPD clinic. Additionally, variation in provider practice may influence oxygen weaning strategies and timing. Lastly, causality cannot be determined in this retrospective study.

In conclusion, we found a median age of weaning off of oxygen to be 12.5 months, however infants who presented with higher oxygen flows at initial outpatient evaluation required longer periods of time to be weaned off supplemental oxygen. Rates of supervised oxygen weaning were lower in certain socioeconomic groups, as well as in children with specific co-morbidities. This may reflect a need for additional education of caregivers by clinicians about the importance of administering oxygen, particularly those groups at higher risk for unsupervised weaning.

Acknowledgments

The authors would like to thank the families who participated in this study. This work received funding from the American Academy of Pediatrics and the Flight Attendant Medical Research and Institute.

Funding source: American Academy of Pediatrics; Flight Attendant Medical Research Institute, Number: NIH RHL114800A.

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Fig. 1.
Kaplan-Meier curve of oxygen weaning age by oxygen flow (n = 154).

Fig. 2.
Location/method of oxygen weaning (n = 137).

TABLE 1

— Study Population

	Entire study population (n = 420)	Ever on home oxygen (n = 154)	Never on home oxygen (n = 266)	P-value
Demographics				
Sex (% male)	59.5	61.7	58.3	0.49
Race/ethnicity (% non-white)	67.6	65.6	68.8	0.50
Gestation (weeks)	26.9 ± 2.8 [22.7, 36.0]	26.1 ± 2.4 [23.0, 35.5]	27.3 ± 3.0 [22.7, 36.0]	<0.001
Birth weight (g)	952 ± 471 [380, 3181] (n = 405)	836 ± 437 [380, 3181] (n = 146)	1018 ± 478 [390, 2830] (n=259)	<0.001
Clinical characteristics				
Age at discharge from NICU (months)	4.1 ± 2.6 [0.1, 24.5] (n = 417)	4.9 ± 3.0 [0.1, 24.5] (n=153)	3.6 ± 2.2 [0.1, 17.1] (n = 264)	<0.001
Age at first visit to pulmonary clinic (months)	7.6 ± 5.6 [0.9, 51.3]	7.4 ± 5.4 [2.5, 51.3]	7.7 ± 5.7 [0.9, 41.6]	0.65
Weight at first visit to pulmonary clinic (kg)	6.0 ± 2.2 [2.5, 18.2] (n = 418)	5.7 ± 2.3 [2.5, 18.2]	6.1 ± 2.1 [2.7, 13.8] (n = 264)	0.13
Gastrostomy tube (% yes)	23.8	34.4	17.7	<0.001
Nissen fundoplication (% yes)	16.2	25.3	10.9	<0.001
Mechanical ventilation at home (% yes)	2.4	3.2	1.9	0.38
Inhaled corticosteroids before age 2 years (% yes)	78.6	85.1	74.8	0.014
Socioeconomic characteristics				
Smoking in home (% yes)	28.5 (n = 418)	26.1 (n=153)	29.8 (n = 265)	0.42
Estimated household income (\$'000s)	62.1 ± 21.4 [15.6, 156.6]	61.2 ± 19.4 [15.6, 108.1]	62.6 ± 22.4 [21.9, 156.6]	0.54
Health insurance (% public)	61.4	61.0	61.7	0.90
Caregiver education (% high school or less)	30.9 (n = 291)	34.8 (n = 115)	28.4 (n = 176)	0.25

Bold values in table are statistically significant.

TABLE 2

—Study Subjects by Oxygen Weaning Age

	Ever On Home Oxygen (n = 154)	Weaned off 12 months of age (n = 72)	Weaned off >12 months of age or still on oxygen (n = 82)	P-value
Demographics				
Sex (% male)	61.7	69.4	54.9	0.06
Race/ethnicity (% non-white)	65.6	66.7	64.6	0.79
Gestation (weeks)	26.1 ± 2.4 [23.0, 35.5]	26.2 ± 2.2 [23.0, 35.5]	26.0 ± 2.6 [23.0, 35.0]	0.69
Birth weight (g)	836 ± 437 [380, 3181] (n = 146)	832 ± 410 [390, 3150] (n = 68)	840 ± 461 [380, 3181] (n = 78)	0.91
Clinical characteristics				
Age at discharge from NICU (months)	4.9 ± 3.0 [0.1, 24.5] (n = 153)	3.8 ± 1.3 [0.1, 7.2]	5.9 ± 3.7 [2.0, 24.5] (n = 81)	<0.001
Age at first visit to pulmonary clinic (months)	7.4 ± 5.4 [2.5, 51.3]	5.5 ± 1.7 [2.5, 10.0]	9.1 ± 6.8 [2.5, 51.3]	<0.001
Weight at first visit to pulmonary clinic (kg)	5.7 ± 2.3 [2.5, 18.2]	5.1 ± 2.0 [3.0, 18.2]	6.3 ± 2.5 [2.5, 15.1]	0.002
Gastrostomy tube (% yes)	34.4	13.9	52.4	<0.001
Nissen fundoplication (% yes)	25.3	11.1	37.8	<0.001
Mechanical ventilation at home (% yes)	3.2	0.0	6.1	0.033
Inhaled corticosteroids before age 2 years (% yes)	85.1	76.4	92.7	0.005
Pulmonary hypertension (% yes)	24.0	13.9	32.9	0.006
Oxygen flow (% >1/4 LPM)	32.5	19.4	43.9	0.001
Unsupervised weaning (% yes)	32.1 (n = 137)	26.4 (n = 72)	38.5 (n = 65)	0.13
Socioeconomic characteristics				
Smoking in home (% yes)	26.1 (n = 153)	20.8	30.9 (n = 81)	0.16
Estimated household income (\$'000s)	61.2 ± 19.4 [15.6, 108.1]	62.7 ± 18.2 [34.3, 105.1]	60.0 ± 20.4 [15.6, 108.1]	0.39
Health insurance (% public)	61.0	55.6	65.9	0.19
Caregiver education (% high school or less)	34.8 (n = 115)	37.3 (n = 51)	32.8 (n = 64)	0.62

Bold values in table are statistically significant.

TABLE 3

—Study Subjects by Oxygen Weaning Method

	Weaned off of oxygen (n = 137)	Supervised weaning (n = 93)	Unsupervised weaning (n = 44)	P-value
Demographics				
Sex (% male)	62.8	64.5	59.1	0.54
Race/ethnicity (% non-white)	65.0	59.1	77.3	0.038
Gestation (weeks)	25.8 ± 2.1 [23.0, 35.5]	25.8 ± 1.9 [23.0, 31.0]	26.0 ± 2.4 [23.0, 35.0]	0.59
Birth weight (g)	794 ± 337 [380, 3150] (n = 131)	768 ± 267 [390, 1790] (n = 88)	847 ± 446 [380, 3150] (n = 43)	0.21
Clinical characteristics				
Age at discharge from NICU (months)	4.7 ± 2.5 [0.1, 14.9]	4.5 ± 2.3 [1.5, 14.3]	5.1 ± 2.8 [0.1, 14.9]	0.17
Age at first visit to pulmonary clinic (months)	6.9 ± 3.4 [2.5, 29.0]	6.6 ± 3.5 [2.5, 29.0]	7.3 ± 3.3 [2.5, 17.2]	0.31
Weight at first visit to pulmonary clinic (kg)	5.6 ± 2.1 [2.5, 18.2]	5.4 ± 2.2 [3.0, 18.2]	5.9 ± 1.9 [2.5, 10.7]	0.22
Gastrostomy tube (% yes)	31.4	26.9	40.9	0.10
Nissen fundoplication (% yes)	21.2	19.4	25.0	0.45
Mechanical ventilation at home (% yes)	2.9	3.2	2.3	0.76
Inhaled corticosteroids before age 2 years (% yes)	85.4	81.7	93.2	0.08
Pulmonary hypertension (% yes)	23.4	17.2	36.4	0.013
Oxygen flow (% >1/4 LPM)	32.1	31.2	34.1	0.73
Weaned after 12 months of age (% yes)	47.5	43.0	56.8	0.13
Socioeconomic characteristics				
Smoking in home (% yes)	24.1	22.6	27.3	0.55
Estimated household income (\$'000s)	62.4 ± 18.9 [15.6, 108.1]	60.6 ± 18.2 [15.6, 108.1]	66.1 ± 20.0 [25.2, 105.1]	0.12
Health insurance (% public)	60.6	53.8	75.0	0.018
Caregiver education (% high school or less)	34.3 (n = 102)	34.3 (n = 70)	34.4 (n = 32)	0.99

Bold values in table are statistically significant.