Bronchopulmonary Dysplasia: When the Very Preterm Baby Comes Home

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Close monitoring for pulmonary hypertension, systemic hypertension and nutritional support are necessary to maximize the growth and development of these high-risk children.

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Abstract

Many infants with severe bronchopulmonary dysplasia (BPD) can be safely managed with oxygen at home. This review covers criteria for home oxygen therapy, monitoring, and weaning protocols for oxygen therapy in the outpatient setting. Although most infants with BPD are weaned from oxygen within a year, they continue to have pulmonary function abnormalities into adolescence. These infants also require evaluation for pulmonary hypertension, systemic hypertension, and a strong focus on adequate nutritional needs for growth.

Introduction

Bronchopulmonary dysplasia (BPD), defined as a need for oxygen at 36 weeks corrected gestational age, affects up to 40% of all preterm infants with birth weights less than 1000 grams.[1,2] The more immature the patient population the higher the risk for BPD. Antenatal steroids and surfactant therapy have decreased mortality in these very immature infants, but BPD has increased because of increased survival. Although often necessary for survival in the smallest infants, mechanical ventilation and lung inflammation are central to the development of BPD.[3-6] Mechanical ventilation at birth stretches the airways, causes airway epithelial injury and differentiation, and diffuse lung inflammation.[7,8] Clinicians are trying to decrease exposure to mechanical ventilation, but BPD rates have not declined substantially with the introduction of less invasive mechanical ventilation.[9]

Improved modes of mechanical ventilation and surfactant replacement therapy have changed BPD from the "Old BPD" described by Northway to a "New BPD".[3,10] The Old BPD was characterized by hyaline membrane formation and epithelial disruption with airway injury, epithelial metaplasia, and fibrosis.[11] The New BPD, in the post-surfactant treatment era (after 1990), is characterized by alveolar simplification, pulmonary microvascular changes, and small airway injury.[12,13] Although the majority of infants with BPD are weaned from oxygen within a year, school-age children diagnosed with moderate to severe BPD continue to have respiratory problems at 6 years of life and changes in lung mechanics persist at least into adolescence.[12-15]

The severity of BPD varies widely amongst the very preterm infants, and the definitions for BPD may need adjusting to better capture the long-term severity of the disease. [16] Some infants will have the diagnosis of mild

BPD at 36 weeks, but go home on room air and taking all feeds by mouth. Other infants will have such severe lung disease they need tracheostomies and continued mechanical ventilation similar to the "Old BPD". This review will focus on the infants with moderate to severe BPD who often go home on nasal cannula oxygen, and the outpatient management needed to optimize their health. Some of these infants are managed by neonatologists in high risk follow-up clinics, others by pulmonologists, and some by their pediatricians.

Home Oxygen: Before Discharge from NICU

Once oxygen requirements are low and the infant is stable, discharging to the home on nasal cannula oxygen is a consideration. There are potential family and financial benefits to sending a child with chronic lung disease home with nasal cannula (NC) oxygen and continuing to wean to room air in the outpatient setting. Our goal for home oxygen therapy is to prevent the effects of chronic hypoxemia, while facilitating improvements in the quality of life and psychological impact for the infant, parents and family offered by the home environment. There is variability in the percent of infants that go home on NC between NICUs, partially due to the multiple things that must be considered before discharge.[17] Determining who goes home with oxygen is based on the child's stability, the parent's ability and the availability of support services in the area that the family lives (Box 1).[18]

Child's Stability

Children being considered for home oxygen should be on <0.5 LPM of NC O_2. [19] The child should have stable oxygen saturations, with saturations that do not fall below 90% for more than 5% of an artifact-free recording period.[20] Although some centers send home infants on > 0.5 LPM these infants are often sicker and have no margin for error during illness.[15,18] Higher flow rates are also often difficult to maintain on portable oxygen tanks. The infant must also have sufficient pulmonary reserve to remain stable during a short-term, accidental disconnection from supplemental oxygen [21]. The child should be able to maintain a minimum saturation of >80% in room air for 30 min before discharge.[19] A determination of what defines a clinically stable child can be debated. Typically if the child has no increased work of breathing, tachypnea or respiratory distress, and has appropriate consistent weight gain, he has a good basis for discharge. [19] An echocardiogram should be performed prior to discharge to assess for pulmonary hypertension and the pulmonary hypertension is stable or improving on the current treatment plan.

Box 1. Criteria for Home Oxygen Therapy

1) Stable on < 1/2L 100% oxygen
- Maintaining saturations greater than 92%
- No apnea requiring intervention for 5 days
- Adequate daily weight gain (20 g/d)

2) Available home health care provider
- Pulse oximetry or apnea monitor
- Home oxygen tanks or oxygen condenser

3) Parental Education Completed
- CPR education and emergency plan in place
- Back-up coverage plan for parents
- Primary medical doctor involved

Parent's Ability

While the child's stability is being assessed, the parent's ability also needs to be assessed. The family needs to feel comfortable with having a child at home that will require extra care and monitoring, and the staff should feel that the family is capable of the additional tasks of home oxygen. They will also need to be capable of managing the medications, oxygen equipment, and home monitor. This ability not only includes the parents, but also includes the other family members and friends that may be involved in the care of this child. Some families will not be comfortable or will not have these abilities, and are poor candidates for home oxygen.[19]

What Needs to be in Place Prior to Discharge

Success after discharge is greatly influenced by how prepared the family is to take the child home on oxygen.[19] Family education for all care givers is required and understanding demonstrated to the NICU staff. An emergency plan needs to be clearly defined and all caregivers are taught infant CPR. For example, if having desaturations or respiratory distress, the care givers may be instructed to increase the oxygen flow, possibly give a nebulizer treatment, call the primary medical provider (PMD) or 911 and know what medical facility to bring the child to. Prior to determining a home plan, conversations with the PMD should include their comfort in co-managing infants on oxygen. Care

givers also need to be educated on the importance of immunizations, influenza vaccine, and RSV prophylaxis. They also need to understand the importance of no smoking around the child while on oxygen therapy and after it is discontinued.

Once the child has been determined to be a candidate for discharge home on supplemental oxygen, arrangements are made for the home medical equipment. Unfortunately, access to appropriate Home Health companies or home nursing can be a limitation in some rural areas. The child is typically sent home on nasal cannula oxygen with portable oxygen tanks (oxygen cylinders) for ease of travel and large oxygen tanks or an oxygen concentrator for in home use.[17] There is no evidence that one oxygen source is better than the other, and often is dependent on availability within a geographic region. Some tanks are generally required as backup for equipment failure or power outage. Equipment education is typically taught by the supplier and includes basic management, the trouble shooting of typical problems, and contact information in the event of equipment failure. A final step before discharge often includes an overnight "rooming in" period for the family and caregivers; which allows them to practice as the solo caregiver while having the security of help from the staff just outside the room.

Monitoring Home Oxygen

Close monitoring of infants on home oxygen is essential and has been done with either apnea/cardiac monitors or pulse oximetry.[22] Although apnea monitors provide some important information, the practical non-invasive method for assessment of oxygenation remains pulse oximetry.[17,22] Previously, the child was sent home on a cardiac/apnea monitor due to pulse oximeters being unavailable and inaccurate with frequent false alarms. As pulse oximeters have improved, oxygen saturations monitoring has become more reliable with stable readings and a preferred form of continuous monitoring.[15] Performing spot oximetry checks in the outpatient setting limits the ability to adequately assess oxygenation needs especially during times that the child may be most vulnerable to hypoxia (feeding, bathing and sleep).[19] Anecdotally, we have not found care givers to be more frustrated by the use of pulse oximetry rather than a cardiac/apnea monitor.

There is controversy about the appropriate target oxygen saturation range for these children. The available evidence suggests that the median oxygen saturation of former preterm infants with chronic lung disease is 95-97%. Chronic hypoxia may contribute to a number of unwanted systemic effects; many which improve when oxygen saturations are maintained over 93%.[17,20,23] Although higher saturations early in life are associated with retinopathy of prematurity, maintaining higher saturations may decrease the progression of ROP and multiple international societies recommend saturations greater than 92% for home oxygen. [17,19,20,23]

Weaning Home Oxygen

Once the child has been discharged, the determination for readiness to wean oxygen begins. Although many infants wean earlier, the average age of weaning is 10 months corrected age.[15] There is very limited research about the appropriate weaning strategy, thus there is a wide range of practices.[17,18,23] Unfortunately, up to a third of infants are weaned from oxygen by their caregivers without medical supervision.[15] Weaning of oxygen therapy is based on clinical assessment, including respiratory status and growth, combined with overnight pulse oximetry results and echocardiogram if pulmonary hypertension is present. If the child is on home medications related to their chronic lung disease (diuretics) we wean these off first. Weaning of albuterol and inhaled corticosteroids is normally done with the input of pediatric pulmonology. Assessment of oxygenation during sleep with either continuous overnight oximetry or polysomnography is recommended when weaning infants from supplemental oxygen.[17,20,23] Overnight oximetry and polysomnography provide more accurate data of oxygenation than spot oximetry checks.[15,17] Spot saturations are not used to wean oxygen due to the potential of missing periods of hypoxia that may occur with sleep and feeding.[15,24] Overnight oximetry is a cost-effective test that is easy to perform in the home as a last weaning step to room air.[20,24] It involves downloading a 12 hour period of oxygen saturation readings from home monitor, and looking for periods of desaturation. A goal of greater than 90% of reading over 98% is often required prior to weaning.[24] However, overnight oximetry cannot rule out obstructive sleep apnea. Therefore, polysomnography in infants can be useful in assessing the degree of upper airway obstruction but the false positive rate may be significant and very little normative data exists. [25] Once it is determined that the child's clinical status and

Box 2. Proposed home oxygen weaning protocol

1. Children are assessed in the Follow-up Clinic every 2-4 weeks.
2. Continuous home pulse oximeters - maintain saturations >93%
3. Once infant determined to be stable, wean oxygen stepwise by 1/8 LPM or 0.1 LPM for each step, pending on the type of flow meter used.
   - Continuous monitoring to evaluate saturations while eating and asleep
   - Instruct family to increase oxygen if saturations are below 93% and to notify the physician managing oxygen (goal minimum saturation level 93-95%)
   - Consider a slower wean for pulmonary hypertension or if growth is stagnant.
4. Infant can first be weaned to room air during awake periods
5. Once stable of room air during the day, perform overnight oximetry test
   - If saturations >90% for 98% of the study, wean to room air
   - Could consider wean if oxygen saturations >90% for 96% of the study with no low desats or if artifact is suspected, except when there are comorbidities (pulmonary hypertension, poor growth, bad ROP)
   - Repeat overnight oximetry study on room air.
6. Once on room air, keep oxygen and pulse ox in the home to use PRN for 3 months or longer (for acute URIs)

oxygen saturations are stable, weaning of oxygen may be started in a stepwise fashion (Box 2). Many institutions, including our own, have used weaning protocols where infants are monitored on room air in the clinic for 30 minutes, then sent home. This form of "room air challenge' could miss desaturations during sleep. Our own practice for weaning oxygen is evolving as more evidence is published, and we have begun to adopt a more comprehensive weaning protocol (Box 2). A current multicenter trial is underway (clinicaltrial.gov NCT01994954) to determine optimal weaning protocols for infants discharged home on oxygen.

Long Term Respiratory Health

Although alveolar simplification is the hallmark of New BPD, small airway injury continues to be prominent in children with a history of BPD.[12,13] Infants discharged on oxygen have higher rates of respiratory medication use in the first 36 months of life.[26] Viral infections in infants with BPD, likely due to increased airway inflammation and narrowing of airways, are a common cause of hospitalization in children under the age of two.[23] School-age children diagnosed with moderate to severe BPD have decreased FEV_1, increased respiratory symptoms, and decreased peak flow measurements at 6 years of life.[13] Changes in pulmonary function testing persist into adolescence and former infants with BPD are more likely to be prescribed asthma medications.[12-14] Although there is some debate about whether preterm infants have a higher rate of "asthma", a recent meta-analysis demonstrated that preterm infants had increased bronchial responsiveness to methacholine challenge or exercise by two fold (OR 1.9; 1.2,2.7) and infants with a history of BPD had an additional 2 fold increase (OR 4.5; 2.7,7.7) compared to term controls.[27]

The airway obstruction is likely due to both a fixed component and a reactive component, which may explain the variable responses infants with BPD have to bronchodilators.[28] There is limited data on efficacy of bronchodilators in the acute treatment of developing BPD and large variations amongst neonatologist in use of bronchodilators, ipratropium (Atrovent), and inhaled steroids like budesonide (Pulmocort). [16,23] Former preterm infants with BPD have an increased incidence of tracheomalacia, which normally resolves by 2 years, and obstructive sleep apnea is 3 to 5 times as common in former preterm infants through school-age than term infants.[28] Fortunately, many of the respiratory symptoms improve over time with additional lung growth.[29] Preterm infants with a history of BPD may require follow-up with pediatric pulmonary specialists.

Pulmonary Hypertension

Infants with BPD have increased risk of pulmonary hypertension (25 to 37% of infants), and may progress to right heart failure if severe. [30] The mortality for infants with untreated pulmonary hypertension beyond 3 months corrected age is roughly 40% within 2 years.[31,32] Screening echocardiograms should be done on infants with established BPD at 36 weeks and then monthly in NICU, and then every 4 to 6 months as outpatients if oxygen requirement persists.[23,33] In infants with BPD and increased PVR, oxygen saturations of 92 to 95% may be appropriate.[33] Inpatient treatment of pulmonary hypertension with BPD includes inhaled nitric oxide,

IV pulmonary vasodilators (flolan) and systemic after load reducers (milronone), and oral medications (sildenafil, bosentan, tadalafil).[34] The most severe cases of pulmonary hypertension are seen in infants requiring continued mechanical ventilation and tracheostomy. Some infants will be discharged home on sildenafil three times a day or tadalafil daily, but these medications may be difficult to get in liquid form from non-compounding pharmacies. Close follow-up with cardiology is necessary for titrating medications and possible needs for cardiac catherization.

Systemic Hypertension

Some infants with BPD have increased systemic blood pressures (>95% for the post-menstrual age) and require medication.[35] Although the pathophysiology of the systemic hypertension is likely multi-factorial, changes in the angiotensin-renin system due to angiotensin converting enzyme 2 in the lung may play a role in BPD. Most infants with hypertension in the NICU requiring treatment will have screening renal ultrasounds and kidney function screening prior to discharge. Infants are treated with a wide variety of medications from diuretics (hydrochlorothiazide, spironolactone) to anti-hypertensive medications (beta blocker, calcium channel blockers, ACE inhibitors).[35] Diuretics for the treatment of the lung disease in BPD have not been demonstrated to have long term benefits [36]. Fortunately, the hypertension associated with BPD typically resolves by 2 years (often by 8 months) and anti-hypertensive medications are weaned or allowed to be outgrown.[37] Hypertension management is often overseen by pediatric nephrology during NICU hospitalization and as outpatient.

Nutrition for Growth

Optimal growth is essential for the infant with BPD to be successfully be weaned from oxygen and to continue the delayed alveolarization that can occur until early adolescence. Infants with BPD often have a higher caloric need, due to increased respiratory effort, and will need additional calorie supplementation (many require 24 to 30 calorie formulas or fortified BM). Energy needs can be 25% higher than infants without BPD, with an average intake of up to 140 kcal/kg/d.[38] One of the criteria for weaning oxygen is adequate growth and weight gain (goal of 20 to 30 grams per day).[39] Although breastfeeding is encouraged, many of these infants will require additional fortified breastmilk or formula to maintain adequate caloric intake and mineral supplementation. Along with additional calories, maintaining adequate micronutrients and vitamins is essential for adequate lung growth. [23,40] As respiratory symptoms improve and growth velocity is maintained off oxygen, caloric intake is often weaned around 1 year of life. Some children with severe BPD will require additional calories drinks (Pediasure, Carnation Instant Breakfast) into early childhood to maintain adequate growth.

Summary

Many infants with moderate to severe BPD can go home on nasal cannula oxygen once they are taking feeds by mouth/g-tube and stable without apnea. Home oxygen therapy requires detailed pre-discharge planning and close follow-up for monitoring and weaning of oxygen therapy. Although the infants normally outgrow their oxygen needs, many of these infants will develop obstructive airway disease. Close monitoring for pulmonary hypertension, systemic hypertension and nutritional support are necessary to maximize the growth and development of these high-risk children.

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Disclosure

None reported. **MM**