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Oxygen Desaturation Complicates Feeding in Infants With Bronchopulmonary Dysplasia After Discharge

Lynn Singer, PhD*; Richard J. Martin, MD*; Suzanne W. Hawkins, MS*; Laura J. Benson-Szekely, MSRD†; Toyoko S. Yamashita, PhD*; and Waldemar A. Carlo, MD§

ABSTRACT. Recurrent episodes of hypoxemia may affect the growth, cardiac function, neurologic outcome, and survival of infants with bronchopulmonary dysplasia (BPD). As oral feeding might stress these infants by compromising pulmonary function even after hospital discharge, we measured oxygen saturation (Sao) via pulse oximetry before, during the initial 10 minutes of, postconceptional age of 43 weeks while the infants were weaning from supplemental oxygen. Studies were done at a mean postconceptional age of 43 weeks while the infants were fed at home by one of their parents. Levels of Sao for the three groups were comparable before and during feeds. After feeding, the infants with BPD had significantly lower mean levels of Sao (84 ± 8% [SD] vs 93 ± 4% and 93 ± 3%, respectively; P < .01). They also spent more time after feeding with an Sao <90% (6 ± 34% of time vs 27 ± 33% for the very low birth weight infant group if there was a history of known drug exposure during pregnancy. We studied infants with BPD who had been recently discharged from the hospital after weaning from supplemental oxygen. We studied 46 infants, including 1 1 infants with BPD, 12 very low birth weight infants, and 23 healthy full-term infants. All infants with BPD had been previously discharged from the hospital after weaning from respiratory distress syndrome or healthy term infants. In another study, infants with BPD who had been recently weaned from oxygen were found to have lower average oxygen saturation levels and more central apnea than preterm VLBW infants without BPD. However, infants in these latter studies were still hospitalized during the assessments. To determine whether differences in episodes of oxygen desaturation between infants with BPD, VLBW infants, and term infants persist beyond discharge, we studied infants with BPD who had been discharged home after appropriate weaning from oxygen while still in the hospital. We also sought to determine whether potentially modifiable aspects of the feeding were related to such desaturation. Therefore, we additionally assessed the relationships of volume of formula, velocity of oral intake, and the relationship of these variables to frequency of desaturation episodes.

MATERIALS AND METHODS

Study Group

We studied 46 infants, including 11 infants with BPD, 12 preterm VLBW infants without BPD, and 23 full-term infants, all matched by postconceptional age (see Table 1). The BPD group comprised preterm infants with respiratory distress syndrome who were treated with supplemental oxygen and/or assisted ventilation for a minimum of 28 days. All infants had some radiographic evidence for chronic lung injury, which could include areas of persistent opacification, hyperinflation, or cystic changes. The VLBW control infants were preterm infants with respiratory distress syndrome who required supplemental oxygen and/or assisted ventilation for no more than 14 days. Infants were excluded from any group if there was a history of known drug exposure during gestation. At the time of study, there was no clinical evidence for any syndrome or major malformation, or for sepsis, significant neurologic problems (other than intraventricular hemorrhage [IVH]), cardiac malformations, or anatomic problems which interfered with feeding.

We studied only infants with BPD who had been discharged home after being weaned from oxygen while still hospitalized. Weaning from oxygen was determined individually by the clinicians responsible for patient care and follows no set protocol, but generally it was performed when average oxygen saturation fell within or exceeded an approximate range of 88% to 90%. Infants were seen as part of a longitudinal follow-up of infants with BPD...
and were studied as near as possible to term, based on their postconceptional ages. This study was approved by the Institutional Review Board for Human Investigations at University Hospitals of Cleveland, OH, and informed consent was obtained from the parent of each infant.

**Recordings**

Oxygen saturation was assessed by noninvasive monitoring during a normal home feeding by one of the infant’s parents. Arterial oxygen saturation (Sao2) was measured via a portable pulse oximeter (Nellcor N-10, Nellcor Inc, Hayward, CA). Pulse oximetry has been shown to be an accurate, simple measure of Sao2 in infants with and without lung disease.10-12 Oxygen saturation values were recorded automatically on a strip chart and were accepted if the pulse rate obtained with the oximeter was consistent with the infant’s heart rate, which was simultaneously recorded.

For each infant, the following parameters were calculated: mean Sao2, highest Sao2 reading, lowest Sao2 reading, percentage of time with readings less than 90%, and percentage of time with readings less than 80%. Oxygen saturation readings were taken for each group at three separate time periods in relation to the feeding, so that changes in oxygenation over those time periods could be examined. Oxygen saturation was sampled at 30-second intervals within each period. Data were analyzed for a 5-minute period before the feeding, for a 5- to 10-minute period immediately after the initiation of feeding, and for a 5-minute period immediately after the feed was completed. For these data, mean values were obtained for each of the three groups of infants.

Parents were asked to feed their infants as was their usual custom, in order to observe the feeding in as typical a context as possible. They were not trained in any specific feeding protocol. Since we were interested in how specific aspects of the feeding might relate to oxygen desaturation, the following information on volume and caloric density of formula consumed was recorded. The total volume in milliliters of formula consumed over the entire feeding time was measured in a standard measuring cup. Length of the feeding to the nearest minute was also recorded. Caloric content was computed by a registered dietician (L.J.B.S.), based on each infant’s individual type of formula. The ratio of kilocalories of feedings, there were no significant differences among groups on any of the readings of Sao2, except the lowest Sao2 reading was significantly less for the BPD group (F = 7.2, P < .01). There were no significant differences in percentages of Sao2 readings <90% and <80%. No VLBW or term infant had periods of desaturation <80% before feedings, while infants with BPD had Sao2 <80% for 7% of the time, although these differences were not significant.

As shown in Table 3, during the initial 10 minutes of feedings, there were no significant differences among groups on any of the readings of Sao2, except for percentage of time with saturations <90% and <80%, which was greater in infants with BPD.

In readings taken immediately after the feedings (see Table 4), infants with BPD were significantly different from both VLBW and term comparison groups, who did not differ from each other on any of the oxygen saturation measures. Mean Sao2 for infants with BPD was 84 ± 8% (SD), and ranged from

**RESULTS**

**Infant Characteristics**

Clinical variables of the study groups are shown in Table 1. Infants with BPD had significantly lower gestational ages than VLBW infants. Infants with BPD also did not differ statistically from VLBW infants in weight at time of study, although their percentiles for height and weight tended to be lower. The groups did not differ in postconceptional age at testing or on maternal social class. As indicated in Table 1, infants with BPD required significantly more oxygen supplementation during the neonatal period. No term infant required any supplemental oxygen or assisted ventilation. Five infants in the BPD group had a clinical history of patent ductus arteriosus, compared with four in the VLBW group. One infant in the VLBW group and five in the BPD group had grades I or II IVH. Four infants in the BPD group had grades III or IV IVH, or PVL, while one VLBW infant had PVL.

**Oxygen Saturation**

Before feedings (see Table 2), mean Sao2, highest Sao2, and periods of desaturation <90% and <80% were not significantly different among groups. However, the lowest Sao2 reading was significantly less for the BPD group (F = 7.2, P < .01). There were no significant differences in percentages of Sao2 readings <90% and <80%. No VLBW or term infant had periods of desaturation <80% before feedings, while infants with BPD had Sao2 <80% for 7% of the time, although these differences were not significant.

**TABLE 1. Medical Characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>BPD (n = 11)</th>
<th>VLBW (n = 12)</th>
<th>Term (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, wk (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational, at birth*</td>
<td>27 ± 2</td>
<td>30 ± 2</td>
<td>39 ± 1</td>
</tr>
<tr>
<td>Postconceptional, at study</td>
<td>43 ± 2</td>
<td>42 ± 2</td>
<td>43 ± 1</td>
</tr>
<tr>
<td>Weight, g (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At birth*</td>
<td>927 ± 276</td>
<td>1219 ± 151</td>
<td>3430 ± 454</td>
</tr>
<tr>
<td>At study*</td>
<td>3114 ± 115</td>
<td>3305 ± 892</td>
<td>4384 ± 762</td>
</tr>
<tr>
<td>Weight, percentile for age (range)</td>
<td>10-25th</td>
<td>25th</td>
<td>50-75th</td>
</tr>
<tr>
<td>Height, percentile for age (range)</td>
<td>5-10th</td>
<td>10th</td>
<td>50-75th</td>
</tr>
<tr>
<td>Duration of supplemental O2, d (mean ± SD)</td>
<td>60 ± 25</td>
<td>6 ± 3</td>
<td>0</td>
</tr>
</tbody>
</table>

* Variables for infants with bronchopulmonary dysplasia (BPD) and those of very low birth weight (VLBW) were significantly different from those for term infants (P < .01).

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Downloaded from www.pediatrics.org at Cleveland Health Sciences on April 10, 2008
TABLE 2. Oxygen Saturation Before Feeding*

<table>
<thead>
<tr>
<th>Variable</th>
<th>BPD</th>
<th>VLBW</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Sao2</td>
<td>93 ± 2</td>
<td>96 ± 3</td>
<td>95 ± 3</td>
</tr>
<tr>
<td>Highest Sao2</td>
<td>98 ± 2</td>
<td>99 ± 2</td>
<td>98 ± 2</td>
</tr>
<tr>
<td>Lowest Sao2</td>
<td>82 ± 4</td>
<td>90 ± 2</td>
<td>90 ± 5</td>
</tr>
<tr>
<td>Percentage of time with Sao2 &lt;90</td>
<td>21 ± 12</td>
<td>7 ± 8</td>
<td>12 ± 18</td>
</tr>
<tr>
<td>Percentage of time with Sao2 &lt;80</td>
<td>7 ± 12</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Values represent mean ± SD. BPD, bronchopulmonary dysplasia; VLBW, very low birth weight; Sao2, arterial oxygen saturation.
† F = 7.2, p < .01; BPD vs VLBW, P < .05; BPD vs term, P < .01.

TABLE 3. Oxygen Saturation During Initiation of Feeding

<table>
<thead>
<tr>
<th>Variable</th>
<th>BPD</th>
<th>VLBW</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Sao2</td>
<td>90 ± 7</td>
<td>94 ± 4</td>
<td>94 ± 3</td>
</tr>
<tr>
<td>Highest Sao2</td>
<td>98 ± 1</td>
<td>98 ± 1</td>
<td>98 ± 1</td>
</tr>
<tr>
<td>Lowest Sao2</td>
<td>75 ± 16</td>
<td>84 ± 8</td>
<td>83 ± 9</td>
</tr>
<tr>
<td>Percentage of time with Sao2 &lt;90</td>
<td>38 ± 26</td>
<td>14 ± 18</td>
<td>20 ± 25</td>
</tr>
<tr>
<td>Percentage of time with Sao2 &lt;80</td>
<td>10 ± 23</td>
<td>2 ± 4</td>
<td>1 ± 2</td>
</tr>
</tbody>
</table>

* Values represent mean ± SD. Abbreviations are explained in the first footnote to Table 2.
† BPD vs VLBW, P < .05.

TABLE 4. Oxygen Saturation Immediately After Feeding

<table>
<thead>
<tr>
<th>Variable</th>
<th>BPD</th>
<th>VLBW</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Sao2</td>
<td>84 ± 8</td>
<td>93 ± 4</td>
<td>93 ± 3</td>
</tr>
<tr>
<td>Highest Sao2</td>
<td>94 ± 5</td>
<td>97 ± 2</td>
<td>98 ± 2</td>
</tr>
<tr>
<td>Lowest Sao2</td>
<td>72 ± 13</td>
<td>87 ± 7</td>
<td>84 ± 6</td>
</tr>
<tr>
<td>Percentage of time with Sao2 &lt;90</td>
<td>64 ± 34</td>
<td>27 ± 33</td>
<td>22 ± 20</td>
</tr>
<tr>
<td>Percentage of time with Sao2 &lt;80</td>
<td>37 ± 28</td>
<td>4 ± 10</td>
<td>4 ± 8</td>
</tr>
</tbody>
</table>

* Values represent mean ± SD. Abbreviations are explained in the first footnote to Table 2.
† BPD < VLBW and term, P < .05.
‡ BPD < or > VLBW and term, P < .01.

73% to 99%, suggesting marked variability within the BPD group. Infants with BPD spent 64% of their time after feeding in desaturation <90%, compared with 27% and 22% of time for VLBW and term infants. Infants with BPD also had significantly longer desaturation episodes <80%, with 37% of readings <80%, in comparison with 4% for VLBW and term infants.

Results of pair-wise comparisons indicated no significant differences on Sao2 measures between time periods for the VLBW and term groups. However, mean Sao2 levels of infants with BPD decreased significantly from the period at the beginning of feeding to the period after feeding (t = 2.78, df = 8, P < .05). This decrement over time and differences among the groups are illustrated in the Figure.

Since there was a higher incidence of IVH/PVL in the BPD group, Pearson’s correlations were also computed for presence and severity of hemorrhage (rated from 0 through 4, and all Sao2 measures. There were no significant relationships between presence of and/or severity of hemorrhage and any of the pulse oximetry readings, suggesting that IVH/PVL were not the precipitants of infants’ desaturation episodes.

Reading Characteristics

As indicated in Table 5, there were no differences among groups in length of feeding, ratio of caloric intake to infant weight, ratio of caloric intake corrected for weight to length of feed, or volume of formula taken during the feed.

Correlation analyses indicated that some behavioral and physical characteristics of the feeding were associated with oxygenation measures only within the BPD group. Increased volume of feed was significantly associated with lower saturation levels during feeding (r = -.66, P < .05) and increased incidence of Sao2 < 90 (r = .72, P < .05) in the BPD group. Higher volume of intake in relationship to infant body weight, and faster feeding of higher volume, were also significantly related to increased incidence of desaturations less than 80% (r = .73, P < .01 and r = .77, P < .01). These relationships were not significant for VLBW or term infants. Length of feed did not relate to any oxygen saturation measures. However, length of feed was associated with infant socioeconomic status as higher social class mothers gave longer feelings (r = -.69, P < .05). For infants with BPD, weight at assessment was unrelated to any oxygenation or feeding measures but was significantly associated with birth weight (r = .63, P < .05).

DISCUSSION

This study employed pulse oximetry to examine the impact of feeding on oxygenation in VLBW infants with and without BPD, compared with healthy term infants. In contrast to prior studies, we assessed infants in the home environment during a normal oral feeding administered by one of their parents. We were primarily interested in assessing whether the episodes of desaturation during feeding observed during prior studies of infants with BPD persisted once infants
had been weaned from supplemental oxygen and discharged from the hospital.

This study demonstrated that preterm infants with BPD differed significantly from both preterm infants without BPD and healthy term control infants in oxygenation levels measured before, during, and after the stress of feeding. In this study, VLBW infants without BPD were comparable with healthy term control infants as they did not differ on any measure of \( \text{Sa}_2 \). However, infants with BPD had more hypoxemia before, during, and immediately after feeding. These findings are congruent with and extend the findings of Garg et al., which indicated that hospitalized infants with BPD experienced unsuspected hypoxia during feeding even in the absence of apnea, bradycardia, or clinical cyanosis. As infants in the present study were studied from 3 to 5 weeks after oxygen weaning and hospital discharge, our findings indicate that desaturations related to feeding are a continuing problem for infants with BPD.

Prior studies have also documented that oxygenation varies with state, especially during sleep and feeding, as reported in infants with BPD, preterm infants, and term healthy infants. Marked declines in oxygenation have been seen with feeding in healthy term and VLBW infants near term. However, the incidence, duration, and extent of desaturations in preterm and healthy term infants in these prior studies are less frequent, shorter in duration, and less severe than observed in infants with BPD.

Because repeated episodes of hypoxia have been suspected to play a role in the increased risk for sudden, unexpected death and in later intellectual deficits in children who have had BPD, it would be important to assess whether clinically significant periods of desaturation continue to occur after hospital discharge. The present data indicate that current clinical practices related to weaning infants with BPD from oxygen need to be reassessed in light of the pronounced variability in oxygen saturation levels in relation to oral feeding.

Sekar and Duke have found that lower levels of oxygen saturation in infants with BPD recently weaned from oxygen are associated with increased episodes of central apnea and periodic breathing densities, which indicates a need for neonatal centers, including our own, to reassess the practices and protocols for oxygen weaning, both prior to and after hospital discharge. It is certainly possible that some infants in this study were weaned prematurely. Furthermore, there may be limitations in the use of average values for oxygen saturation in determining the need for supplemental oxygen. Perhaps future studies could allow randomization of infants to protocols for oxygen administration to identify standardized procedures indicating their readiness for weaning.

Our study also suggests that some behavioral and physical characteristics of the feeding, such as increased volume and faster feeding, are related to increased incidence of severe desaturations in infants with BPD or term infants. There is significant variability for all infants in the volume of formula taken at one feeding. For infants with BPD, however, increased volume and faster feeding were associated with lower oxygen saturation levels, suggesting that clinical observations of slower feeding in infants with BPD may be related to attempts of the infant to minimize desaturation. Individualized approaches to intervention could include assessments of care giver-infant interaction during feeding to determine whether care givers can learn ways to “slow down” an infant’s feeding through frequent pauses or through alteration of nipple size. Whether such behavioral changes might prevent desaturation episodes in infants with BPD requires further investigation. In addition, home oxygen should be considered for feedings in selected children who do not gain weight adequately, demonstrate marked and prolonged saturations, and are difficult feeders secondary to hypoxia.

Within this sample of BPD infants, desaturations were unrelated to neurologic status; however, future studies should explore the possibility that severity of neurologic problems might bear some relationship to hypoxemic episodes. Gastroesophageal reflux, not clinically noted in our BPD group, might also be a factor to be assessed in other studies. Longitudinal investigations of oxygenation in infants with BPD across a variety of behavioral states are necessary to assess the correlates and potential sequelae of desaturation episodes in such infants.

ACKNOWLEDGMENTS

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RICKETS AND ITS TREATMENT IN THE UNITED STATES IN 1847

As late as 1872 the American medical literature was singularly deficient in mentioning rickets. The prevalent opinion among American physicians was that rickets was largely a disease of the Old World. For that reason, the short description of rickets and its treatment by Dr. James Ewell in 1847 is one of the first to be published in the United States.

[Rickets] Consist in an enlargement of the head, belly, and joints, flattened ribs, and general emaciation, with a bloated or florid countenance. The disorder generally takes place from six months to two years of age, and arises either from unhealthy parents, or from the children being improperly nursed, kept wet, dirty, in a close damp air, without due exercise.

Weakness and relaxation being the cause of the complaint, its remedy must, of course, be to promote digestion, and to brace and strengthen the solids. Hence a nutritious and cordial diet, with exercise in the country air, is indispensable. Along with this, the cold bath and tonic medicines, as bark [quinine], Columbo [Frazier carolinensis], and steel, to warm and invigorate the constitution, are peculiarly proper; but they could not be entered upon, without previously purging with calomel and jalap. The tincture of rhubarb should also be occasionally employed, to keep the bowels in a regular state. However, nothing will be found more effectual in recovering the patient, than a generous diet and cold bathing, particularly in salt water. Sea bathing constitutes, perhaps, the most promising remedy in this disease.

REFERENCES


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