Lower Oxygen Saturation Alarm Limits Decrease the Severity of Retinopathy of Prematurity

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PURPOSE To determine whether lowering oxygen saturation alarm limits for infants at risk for retinopathy of prematurity (ROP) reduces its incidence and/or severity.

METHODS Oximetry alarm limits were lowered to 85% and 93% for all infants with a birth weight 1250 g or less and/or gestational age 28 weeks or less, and maintained until 32 weeks’ postmenstrual age or until oxygen saturations were consistently greater than 93% in room air. The new policy was effective for infants born on or after June 1, 2003. ROP data were prospectively collected, and we compared the rate and severity of ROP in the year after the oximeter alarm policy change to the rates in the immediately preceding 3 years.

RESULTS In the year after the oximeter alarm limit policy change, 4 of 72 infants developed prethreshold ROP compared with 44 of 251 infants in the previous 3-year epoch (17.5% vs 5.6%, p = 0.01). Similarly, only 6 of 144 eyes developed prethreshold ROP in the year after the policy change, compared with 84 of 502 in the previous 3 years (16.7% vs 4.2%, p = 0.001).

CONCLUSIONS A simple change in oximeter alarm parameters in the first weeks of life for infants with a birth weight 1250 g or less may decrease the incidence of prethreshold ROP. (JAPOS 2006;10:445-448)

T here is increasing evidence that, in the early neonatal course, relative hyperoxia in very low birth weight (VLBW) infants, especially when alternating with periods of hypoxia, contributes to the development of retinopathy of prematurity (ROP). Although the pathogenesis of ROP is multifactorial, the role of oxygen continues to be studied, and the optimal level of oxygenation for infants after premature birth is yet unknown.1

Several studies have attempted to address the role of oxygen in the development of ROP early or late in the neonatal course. Although early cohort studies demonstrated that blindness from ROP was associated with increased duration of oxygen exposure,2 subsequent restrictions in oxygen treatment led to increased mortality and neurologic morbidity.3 Recent retrospective and observational studies4–7 have suggested that targeting lower oxygen saturations from the delivery room and through the first few weeks of life may be beneficial for reducing the severity of ROP or need for retinal ablative therapy, without increasing the incidence of bronchopulmonary dysplasia (BPD) or neurologic sequelae. Some neonatal intensive care units (NICUs) have therefore chosen to target lower oxygen saturation ranges than historically used in very low birth weight infants. Surveys of NICU policies on oxygen administration and monitoring continue to reveal wide ranges in oxygen saturation targets, and compliance with oxygen delivery policies.7,8

After review of the available data, the oxygen saturation alarm limit policy in the Brigham and Women’s Hospital NICU was modified to target a slightly lower oxygenation range than used previously in infants at highest risk for ROP. The primary objective of this study was to compare the incidence and severity of ROP in all infants screened and discharged home from the Brigham and Women’s Hospital NICU before and after the change in policy lowering the oxygen saturation alarm limits for infants with a birth weight 1250 g or less and/or 28 weeks gestational age or less. A secondary objective was to evaluate visual outcomes for those infants requiring treatment, as an additional indicator of ROP severity.

Methods

Before June 1, 2003, oxygen saturation alarm limits at the Brigham and Women’s Hospital NICU were set at 87% and 97% for all infants, without a specified target range. Oximetry alarm limits were lowered on June 1, 2003, to 85% and 93% for all infants with a birth weight 1250 g or less and/or gestational age 28 weeks or less. Target oxygen saturations were set at 90% to 92%. All infants were monitored throughout the study period using the same oximetry technology (Masimo®; Masimo Corp., Irvine, CA). At 32 weeks’ postmenstrual age, alarm limits were

DOI:10.1016/j.jaapos.2006.04.010
Table 1. Rates of ROP and prethreshold ROP by study year

<table>
<thead>
<tr>
<th>Screening year by DOB</th>
<th># Infants eligible</th>
<th>Mean GA (weeks)</th>
<th>Mean BW (grams)</th>
<th># Infants with any ROP</th>
<th># Infants with PT (%)</th>
<th># Eyes with PT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/1/00–5/31/01</td>
<td>81</td>
<td>27.0</td>
<td>897</td>
<td>49 (60.0)</td>
<td>20 (23.8)</td>
<td>36 (22.2)</td>
</tr>
<tr>
<td>6/1/01–5/31/02</td>
<td>77</td>
<td>27.3</td>
<td>931</td>
<td>35 (45.5)</td>
<td>9 (11.1%)</td>
<td>18 (11.6)</td>
</tr>
<tr>
<td>6/1/02–5/31/03</td>
<td>93</td>
<td>27.5</td>
<td>927</td>
<td>47 (60.5)</td>
<td>15 (16.1%)</td>
<td>30 (16.1)</td>
</tr>
<tr>
<td>6/1/03–5/31/04</td>
<td>72</td>
<td>27.3</td>
<td>945</td>
<td>28 (38.9)</td>
<td>4 (5.6)</td>
<td>6 (4.2)</td>
</tr>
</tbody>
</table>

GA: gestational age; BW: birthweight; PT: prethreshold retinopathy of prematurity; ROP: retinopathy of prematurity

We reviewed data from a 4-year period for all inborn infants who survived to ROP screening and were not transferred to another nursery before their discharge home. The proportion of infants transferred was stable across the years, with 72 of 76 (94.7%) eligible for this study in the year after the policy change, and 251 of 266 (94.5%) eligible from the preceding 3 years. Rates and severity of ROP were compared for the infants born in the year after the oxygenation policy change with infants born during the previous 3 years who were administered supplemental oxygen under the old policy. Statistical analysis was performed using Fisher’s exact test for rates of ROP and prethreshold between groups, and using a t-test for birth weight comparisons. Rates of laser treatment and visual outcomes were compared as secondary indicators of ROP severity. Approval for this study was given through the Brigham and Women’s Hospital Human Research Committee.

Results

Table 1 shows the number of eligible infants per study year. Mean gestational age at birth and birth weight were similar across the years studied. The overall mean gestational age for the group with higher alarm limits was the same (27.3 weeks) as the mean gestational age for the group with lower alarm limits (27.3 weeks). The mean birth weights were also similar for the two groups (919 g vs 945 g, p = 0.43), and the proportion of screened infants with a birth weight less than 1000 g did not vary significantly.

After the oxygenation policy change, there was a 68% reduction in prethreshold ROP (p = 0.01) compared with the previous 3-year epoch (Table 2). Only 5.6% (4/72) of the screened infants for this study reached prethreshold ROP in the year after the oxygenation policy change, compared with 17.6% (44/251) of infants who developed prethreshold ROP or greater in the previous 3 year epoch. Similarly, only 6 of 144 eyes (4.2%) developed prethreshold ROP with lower alarm limits, compared with 44 of 501 (16.7%) with the higher alarm limits (p = 0.001). There was also a lower incidence of any ROP for infants after the policy change (38.9% vs 52.2%), but it was not statistically significant (p = 0.06).
Our results are similar to those reported by Chow et al. In this study, a coincident decrease in the incidence of severe ROP was observed after institution of a comprehensive oxygen management policy designed to limit episodes of hyperoxia and hypoxia in VLBW infants. This policy included initiation of oxygen saturation monitoring at birth, lowering of oxygen saturation alarm limits, written guidelines for changing of $FiO_2$ in response to oximeter readings, and specifically designated staff to care for VLBW infants. Our study differed from this report in that we changed only our oximetry alarm limits and target saturations for VLBW infants, with other aspects of care remaining the same. We observed similar effects on the incidence of ROP severity with these simple changes in clinical practice.

We compared rates of any prethreshold ROP because of the changes in treatment recommendations over the years compared. In the first years of this study, under the greater alarm limits, some eyes that were categorized as “high risk” by the RM-ROP2 program may have been treated if the infant was a participant in the ETROP randomized trial of early treatment for prethreshold ROP. Other eyes were treated only if threshold ROP was reached. No eyes with low-risk prethreshold ROP were treated. In the final year of the study, under the lower alarm limits, eyes were treated only if Type 1 prethreshold ROP developed. No eyes were treated for Type 2 prethreshold. Although high-risk prethreshold as determined by RM-ROP2 analysis and clinical Type 1 prethreshold are not equivalent, and although the numbers for comparison are small, the favorable outcome rate appears to be much better, which may represent less aggressive ROP.

Several large, randomized studies have been conducted to address the effects of targeting different oxygen saturation later in the neonatal course on the severity of ROP. The Supplemental Therapeutic Oxygen for Prethreshold ROP Trial (STOP-ROP) and the Benefits of Oxygen Saturation Targeting Trial (BOOST) showed that supplemental oxygen with higher oxygen saturation ranges after ROP has developed later in the neonatal course may reduce progression of existing retinopathy and need for retinal ablative therapies for some infants. Infants in the higher saturation groups had more adverse pulmonary events (STOP ROP) or required longer supplemental oxygen after discharge home (BOOST), but there was no difference in growth, mortality, or neurologic outcomes. We followed STOP ROP guidelines regarding consideration of supplemental oxygenation for infants who developed prethreshold ROP without plus disease, but because

### Discussion

Oxygen administration is a necessary therapy for VLBW infants, but the optimal and safest level of oxygen saturation is unknown. NICU policies on oxygen administration, oximetry alarm settings, and monitoring vary widely. Many NICUs attempt to target oxygen saturations of 90% to 95%, with lower alarm limits set as low as 75%, and upper limits as high as 100%. Our NICU policy did not fall at either end of this spectrum, and we instituted only a small change in a select group of patients. Our institution changed the oximetry alarm settings as well as specifying a target range only for infants at greatest risk of developing severe ROP. Attention was also given to limiting extreme fluctuations in oxygenation levels, when possible. Although compliance with these policy changes was not monitored, there was a coincident, significant reduction in the rate of prethreshold or greater ROP in our patient population.
this occurred later in the neonatal course and was applied across the study years, this would not have confounded our findings regarding the development of prethreshold ROP.

This study was limited in that we did not attempt to control or evaluate other therapeutic variables or outcomes. No other major changes in neonatal care in our NICU occurred during this period; however, it is possible that other more minor changes in care that were not assessed affected the incidence and severity of ROP. In addition, compliance with the oxygen saturation alarm limits and target saturations were not assessed, which may have limited the results. We changed the oxygen saturation policy with an aim to potentially reduce the severity of ROP, but did not follow patients to evaluate or compare neurologic outcomes or assess rates of cortical visual impairment, and these data were not available. Because we used historical controls, we cannot ensure comparability between the groups. Only 1 year of data is available for comparison to previous years; therefore, longer-term data collection is necessary to determine whether the effect of lowering oxygen saturation limits persists over time.

Our experience suggests that a simple change in oxygenation parameter practice in the first weeks of life for VLBW infants may be associated with a dramatic decrease in the incidence of prethreshold ROP and lower rates of unfavorable visual outcomes caused by ROP. Although infants in this study appeared to have derived ophthalmologic benefit from lower oxygen saturation alarm limits and targeted saturations, a large randomized trial would more adequately assess the short and long-term benefits, and potential risks, of lowering oxygen saturation targets in very low birth weight infants particularly with respect to neurologic outcome.

References