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Room-Air Versus Oxygen Administration for Resuscitation of Preterm Infants: The ROAR Study

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Room-Air Versus Oxygen Administration for Resuscitation of Preterm Infants: The ROAR Study

WHAT'S KNOWN ON THIS SUBJECT: The superiority of room air over 100% oxygen for resuscitating asphyxiated term and near-term newborns has been demonstrated. However, results of studies of preterm infants have indicated that room-air resuscitation may not be appropriate for this population.

WHAT THIS STUDY ADDS: Resuscitation of preterm infants starting with 100% oxygen followed by frequent titration was most effective at achieving a target oxygen saturation while avoiding hyperoxemia. Treatment-failure rates were highest for those resuscitated with room air despite rapid titration of oxygen.

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KEY WORDS
oxygen, newborn, resuscitation

ABBREVIATIONS
SpO_2—transcutaneous oxygen saturation
FiO_2—fractional inspired oxygen concentration
CI—confidence interval

This trial has been registered at www.clinicaltrials.gov (identifier NCT00356902).

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abstract

OBJECTIVE: We conducted a blinded, prospective, randomized control trial to determine which oxygen-titration strategy was most effective at achieving and maintaining oxygen saturations of 85% to 92% during delivery-room resuscitation.

METHODS: Infants born at 32 weeks' gestation or less were resuscitated either with a static concentration of 100% oxygen (high-oxygen group) or using an oxygen-titration strategy starting from a concentration of 100% (moderate-oxygen group), or 21% oxygen (low-oxygen group). In the moderate- and low-oxygen groups, the oxygen concentration was adjusted by 20% every 15 seconds to reach a target oxygen saturation range of 85% to 92%. Treatment failure was defined as a heart rate slower than 100 beats per minute for longer than 30 seconds.

RESULTS: The moderate-oxygen group spent a greater proportion of time in the target oxygen saturation range (mean: 0.21 [95% confidence interval: 0.16–0.26]) than the high-oxygen group (mean: 0.11 [95% confidence interval: 0.09–0.14]). Infants in the low-oxygen group were 8 times more likely to meet the criteria for treatment failure than those in the high-oxygen group (24% vs 3%; $P = .022$). The 3 groups did not differ significantly in the time to reach the target oxygen saturation range.

CONCLUSIONS: Titrating from an initial oxygen concentration of 100% was more effective than giving a static concentration of 100% oxygen in maintaining preterm infants in a target oxygen saturation range. Initiating resuscitation with 21% oxygen resulted in a high treatment-failure rate. *Pediatrics* 2011;128:e374–e381

Attitudes toward oxygen use during newborn resuscitation have changed considerably over the last few years. This is a direct result of several studies[1–7] that did not show a benefit to resuscitating newborns with 100% oxygen versus room air. The population of these important studies consisted mostly of term infants who were described as asphyxiated. Although the individual studies did not demonstrate an impact on mortality, 4 meta-analyses have revealed a significant survival benefit for using static concentrations of room air compared with 100% oxygen when resuscitating asphyxiated newborns.[8–12] The relative risk of death favoring room-air resuscitation was between 0.57 and 0.71 in all infants and 0.51 for the subgroup of infants less than 37 weeks' gestation.[10] More recently, room-air resuscitation studies have focused on the preterm population and have supported the practice of preventing hyperoxia. Most notably, Vento et al[13] found that initiating resuscitation with 30% versus 90% oxygen for infants 28 weeks' gestation or less significantly reduced the risk of developing bronchopulmonary dysplasia.

There are important differences in the challenges facing preterm infants and asphyxiated term infants at birth. Preterm infants must overcome difficulties in gas exchange resulting from surfactant deficiency, incomplete lung development, inadequate respiratory drive, and poor clearance of lung fluid, concerns that are less common in the term population and may make the use of static concentrations of room air problematic. Therefore, applying findings from earlier studies in asphyxiated term infants to the preterm population may not be appropriate. Resuscitation studies of preterm infants recently have been published that highlight these challenges. In every study to date, it was common for infants in the low-oxygen group to require an increase in their inspired oxygen concentration to achieve a target oxygen saturation, with 2 studies reporting that this occurred in more than 90% of infants.[13–16] Although these studies demonstrate that a static concentration of room air during resuscitation of preterm infants is not appropriate, they do show that the titration of oxygen can be effectively guided by pulse oximetry in the delivery room.

The objective of this study was to determine which of 3 oxygen-titration strategies was best at maintaining a target transcutaneous oxygen saturation ($SP0_2$) range of 85% to 92% during delivery-room resuscitation. We hypothesized that infants initially resuscitated with 21% oxygen would remain in the target $SP0_2$ range for the greatest proportion of time during resuscitation. This study was conducted before the publication of studies showing that preterm infants often require supplemental oxygen during resuscitation.[13–16] The mean oxygen saturation in the umbilical vein after an uncomplicated delivery is 53% and, on average, takes 5 minutes to reach 85% to 92%.[17–22] For the present study, we chose to target the $SP0_2$ range observed at 5 minutes of age in healthy term infants transitioned in room air during the resuscitation of preterm infants. There were no recommendations regarding the best $SP0_2$ range to target during resuscitation of both term and preterm infants at the time this study was conducted. The 2005 International Liaison Committee on Resuscitation guidelines that were current during the study recommended the use of a static concentration of 100% oxygen during resuscitation of preterm infants.

METHODS

The study was conducted at a level III center responsible for high-risk deliveries for 1.3 million people (Foothills Medical Centre) from January 2005 until September 2007. Our local research ethics board approved this study. Because there was equipoise regarding the 3 treatment arms, we were permitted to obtain consent from parents after the intervention for inclusion of collected data and ongoing monitoring until discharge.

An investigator was on call continuously for the duration of the study. Infants who were 32 completed weeks' gestation or less at birth and inborn at the study center were eligible. Infants with lethal anomalies, risk of persistent pulmonary hypertension (ie, presence of oligohydramnios, meconium at delivery), antenatally diagnosed cyanotic congenital heart disease, or hemoglobinopathy were excluded from study enrollment. Subsequent to randomization, infants not requiring assisted ventilation during resuscitation, per Neonatal Resuscitation Program guidelines, were excluded from the analysis. Assisted ventilation was defined as the provision of intermittent positive-pressure ventilation or continuous positive airway pressure delivered via facemask and/or endotracheal tube. Gestational age assessment was based on the results of the 11-week antenatal ultrasound or, in the absence of an early ultrasound, the date of the last known menstrual period.

Apart from titrating supplemental oxygen, all resuscitation procedures, including the provision of assisted ventilation, followed the Neonatal Resuscitation Program guidelines that were current at the onset of the study.[23] Early surfactant administration in the delivery room for infants born at 27 weeks' gestation or less is practiced at our institution. An investigator placed an oximetry probe on the right wrist (preductal position) and a sensor (Datex-Ohmeda [GE Healthcare, Milwaukee, WI]) in line between the bag-

ging unit and the facemask/endotracheal tube immediately after birth for continuous collection of oxygen saturations and pulmonary monitoring for end-tidal carbon dioxide concentrations, inspired oxygen concentrations, peak inspiratory pressure, positive end-expiratory pressure, and respiratory rate.

Titration of the fractional inspired oxygen concentration (F_{IO_2}) was controlled by the investigator as follows:

1. High-oxygen group: static concentration of 100% oxygen during assisted ventilation;
2. Moderate-oxygen group: assisted ventilation started with 100% oxygen; and
3. Low-oxygen group: assisted ventilation started with 21% oxygen.

In the moderate- and low-oxygen groups, the F_{IO_2} was adjusted in increments of 20% every 15 seconds if the SP_{O_2} was outside of the target oximetry range of 85% to 92%, followed by smaller adjustments of 5% to 10% to maintain the SP_{O_2} within the target range.

Treatment failure was defined as a heart rate slower than 100 beats per minute for longer than 30 seconds. In these cases, the F_{IO_2} was immediately increased to 100% for the remainder of the resuscitation. Chest compressions were started if tactile stimulation and assisted ventilation failed to increase the heart rate to faster than 60 beats per minute within 30 seconds. In instances where the pulse oximeter did not register a stable value, resuscitation continued at the current F_{IO_2} as long as the heart rate was 100 beats per minute or faster. Resuscitation was defined as starting at the time of birth and ending when the infant left the delivery room.

The primary outcome was the proportion of resuscitation time spent in the target SP_{O_2} range of 85% to 92%. The short-term secondary outcome measures were the proportion of total resuscitation time spent outside the target SP_{O_2} range, oxygen exposure, F_{IO_2} at the end of resuscitation, rate of intubation, and resuscitation duration. Total oxygen exposure was calculated to produce a standardized estimate of exposure to the equivalent of 100% oxygen represented as liters of 100% oxygen per kilogram body weight: (inspired gas-flow rate [L/minute] $\times$ duration of resuscitation [minutes] $\times$ F_{IO_2})/birth weight (kilograms). Other secondary outcome measures were survival at discharge, length of mechanical ventilation, length of hospital stay, and incidence of bronchopulmonary dysplasia (defined using the Shennan criteria).[24]

The sample size estimate was calculated using PASS sample-size software (NCSS, Kaysville, UT) on the basis of the primary outcome. A sample size of 108 infants (36 in each group) was required to detect a difference of 30% between 2 adjacent means (80%, 50%, and 20% of the resuscitation time spent in the target SP_{O_2} range) with 80% power at the 5% level of significance (2-tailed).

We used a permuted-block randomization design with random block sizes of 3 and 6 using a computer-generated randomization schedule. The allocation sequence was constructed by a nonclinician who was not involved in the study and maintained possession of the allocation sequence in a locked drawer. Concealment of allocation was via serially numbered, sealed, opaque envelopes that were opened in a sequential manner immediately before the delivery of a potentially eligible infant by the study investigator. Randomly assigned infants who did not subsequently meet the inclusion criterion of requiring assisted ventilation were not included for statistical analysis.

The biostatistician, data collector, and those providing resuscitation and ongoing care for the infants were blinded to the intervention. To facilitate blinding, a custom research cart housed the monitoring equipment and oxygen blender, which were only visible to the study investigator. For infants randomly assigned to the high-oxygen group, the investigator made sham adjustments to the oxygen blender.

Infants receiving the study intervention were analyzed in the group to which they had been randomly assigned. Comparison of the mean proportion of time spent in the target SP_{O_2} range of 85% to 92%, defined as the time spent in the target SP_{O_2} range divided by the duration of resuscitation, was performed for all 3 groups. A Kruskall-Wallis test was used because the data violated the assumptions of similar variances in the groups. Secondary outcomes and groups characteristics were summarized via means (SD) or medians (interquartile range), as appropriate, for continuous variables and via proportions for categorical variables; 95% confidence intervals (CIs) were calculated in all cases. Where pairwise comparisons were of interest, any significant results were taken as indications of potential association, and corrections for multiple comparisons were used (Tukey honest differences for mean comparisons and Benjamini-Hochberg for proportions).

RESULTS

We enrolled 106 infants; refer to Fig 1 for a description of participant flow. The high number of missed eligible deliveries was largely a result of our inability to arrive at the bedside before the delivery on evenings and weekends. Participants were followed until discharge from the hospital. Baseline demographic data are presented in Table 1. A summary of respiratory inter-

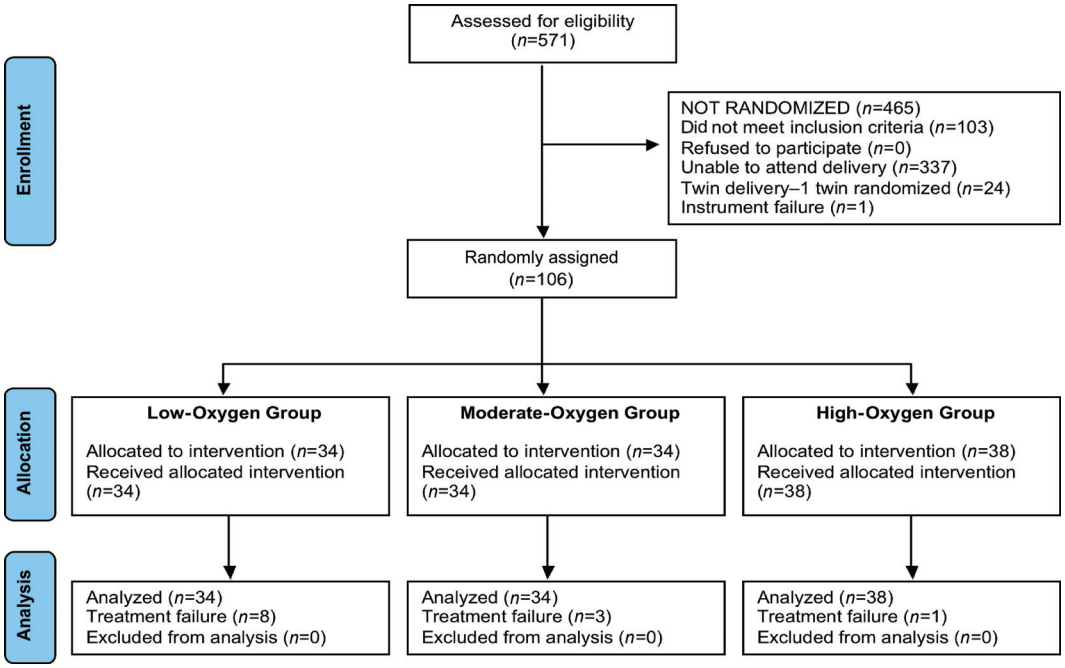

FIGURE 1
Trial flow.

ventions during resuscitation is provided in Table 2.

Primary Outcome

The mean proportion (mean [95% CI]) of time spent in the target SpO_2 range of 85% to 92% was significantly higher in the moderate-oxygen group (mean: 0.21 [95% CI: 0.16–0.26]) than in the high-oxygen group (mean: 0.11 [95% CI: 0.09–0.14]). The low-oxygen group (mean: 0.16 [95% CI: 0.13–0.20]) did not differ significantly from either the moderate-oxygen or high-oxygen groups. The results are presented in Fig 2. There were no statistically significant differences between the 3 groups for the time to reach the target SpO_2 range (low oxygen versus high oxygen: $P = .056$, low oxygen versus moderate oxygen: $P = .159$, moderate oxygen versus high oxygen: $P = .99$) (Fig 3). Oxygen saturations over the first 10 minutes of resuscitation are displayed in Fig 4.

TABLE 1 Baseline Characteristics

	Low-Oxygen Group ($N = 34$)	Moderate-Oxygen Group ($N = 34$)	High-Oxygen Group ($N = 38$)
Gestational age, mean (95% CI), wk	29 (28–30)	29 (28–30)	28 (28–29)
Birth weight, means (95% CI), g	1242 (1092–1391)	1231 (1091–1371)	1151 (1017–1285)
Female/male ratio, proportion (95% CI)	16:18	22:12	20:18
Cord pH, means (95% CI)	7.29 (7.27–7.31)	7.28 (7.25–7.31)	7.30 (7.28–7.32)
Antenatal steroids, proportion (95% CI)	0.85 (0.73–0.97)	0.85 (0.74–0.97)	0.81 (0.67–0.92)
1-min Apgar score, median (interquartile range)	6 (2.5)	6 (3.0)	7 (2.5)

TABLE 2 Respiratory Parameters

	Low-Oxygen Group	Moderate-Oxygen Group	High-Oxygen Group	P
Peak inspiratory pressure, mean (95% CI), cm H_2O	31 (25–37)	34 (27–40)	32 (25–39)	>.05
Rate of positive pressure, mean (95% CI), breaths per min	57 (44–69)	42 (32–52)	40 (28–51)	>.05
End-tidal CO_2 concentration, mean (95% CI)	18 (16–20)	18 (16–20)	18 (16–20)	>.05

Secondary Outcomes

Proportion of Time Outside the Target SpO_2 Range (Fig 2)

The high-oxygen group spent a significantly greater proportion of time above the target SpO_2 range than both the low- and moderate-oxygen groups (low-oxygen mean proportion: 0.23 [95% CI: 0.18–0.27], moderate-oxygen mean proportion: 0.28 [95% CI: 0.23–0.33], and high-oxygen mean proportion: 0.49 [95% CI: 0.42–0.56]). The proportions of infants in the target SpO_2 range at specific time points are presented in Table 3. At 10 minutes, both the low- and moderate-oxygen groups had significantly higher proportions of infants in the target SpO_2 range than the high-oxygen group ($P = .02$).

At 5 minutes, 64.9% of infants in the high-oxygen group had a SpO_2 higher

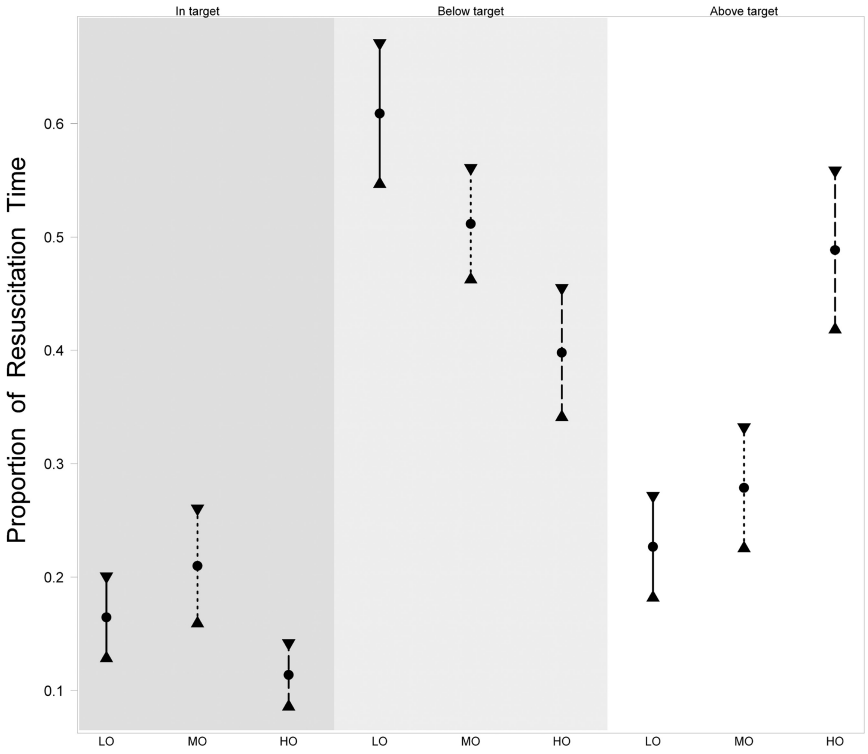

FIGURE 2

Proportion of resuscitation time spent in the target SPO_2 range. LO indicates low oxygen; MO, moderate oxygen; HO, high oxygen.

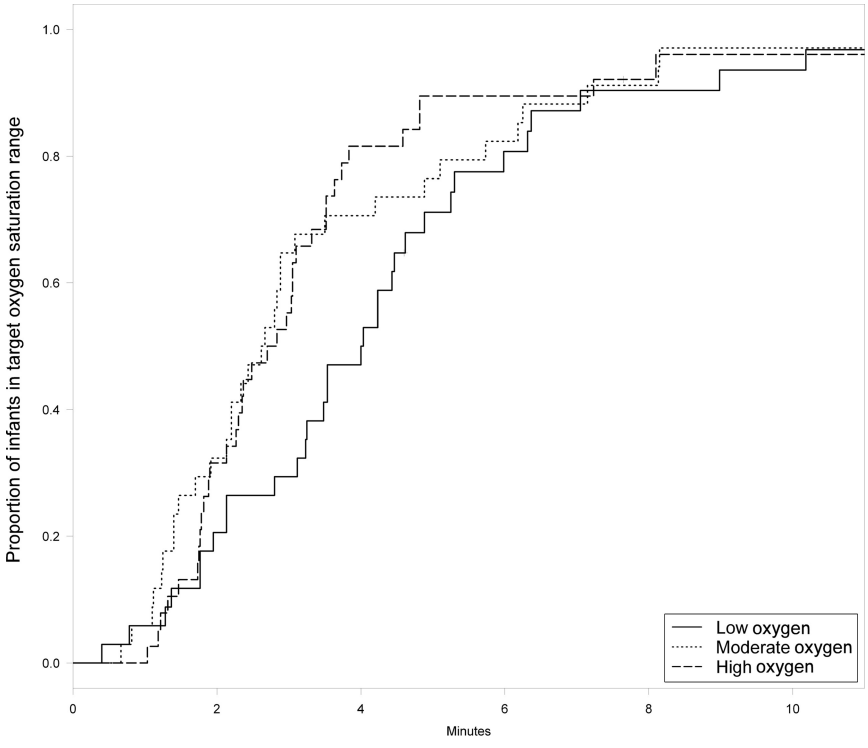

FIGURE 3

Kaplan Meier curve for time to reach target oxygen saturation range of 85% to 92%. Differences between the 3 groups were not statistically significant ($P > .05$).

than 92% compared with 37.5% in the low-oxygen group ($P = .03$) and 36.7% in the moderate-oxygen group ($P < .01$). By 10 minutes, 78.4% of infants in the high-oxygen group had a SPO_2 higher than 92% compared with 33.3% in the low-oxygen group ($P < .01$) and 34.4% in the moderate-oxygen group ($P < .01$). Differences between the moderate- and high-oxygen group were not significant ($P = .9$) at both time points.

The low-oxygen group spent the greatest portion of the resuscitation time below the target SPO_2 range compared with both the moderate- and high-oxygen groups (low-oxygen mean proportion: 0.61 [95% CI: 0.55–0.67], moderate-oxygen mean proportion: 0.51 [95% CI: 0.46–0.56], and high-oxygen mean proportion: 0.40 [95% CI: 0.34–0.45]).

Oxygen Exposure

Refer to Table 4.

Treatment Failure

The mean proportions (95% CIs) of infants meeting the criteria for treatment failure were low oxygen: 0.24 (0.09–0.38), moderate oxygen: 0.09 (0.0–0.21), and high oxygen: 0.03 (0.0–0.08). More infants in the low-oxygen group met the criteria for treatment failure than infants in the high-oxygen group ($P = .022$). One infant (low-oxygen group) required chest compressions. Treatment failure occurred, on average, at 3.7 minutes in the low-oxygen group, at 4.6 minutes in the moderate-oxygen group, and at 2.6 minutes in the high-oxygen group (1 case). Other secondary outcomes are presented in Table 5.

DISCUSSION

We report a blinded, randomized control trial comparing 3 oxygen-titration strategies for the resuscitation of preterm infants. At the start of this trial, Neonatal Resuscitation Program

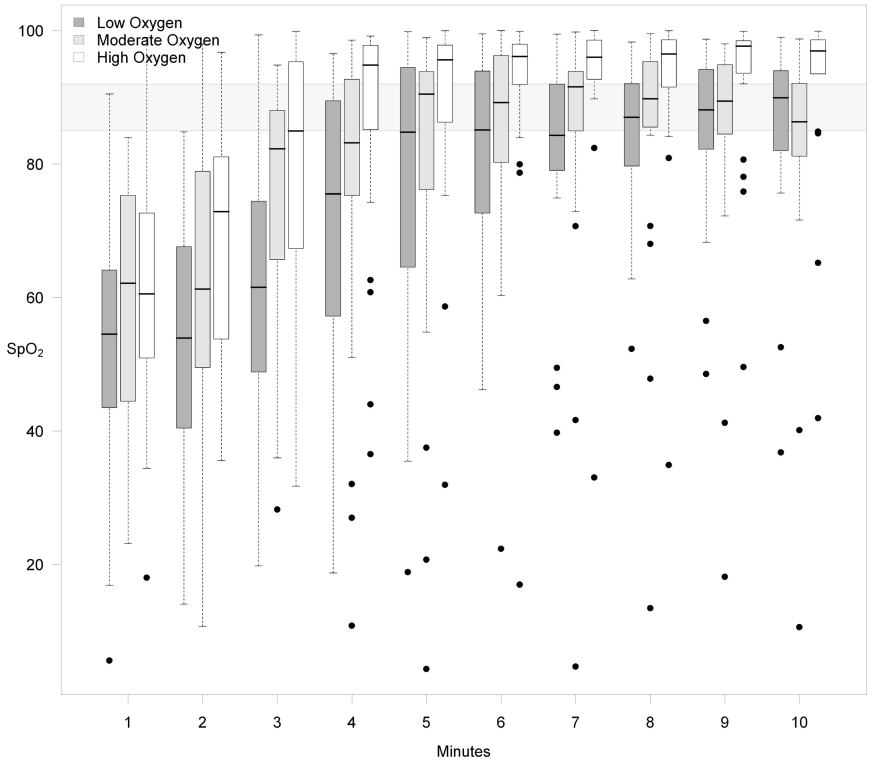

FIGURE 4
Oxygen saturations during resuscitation. The shaded region indicates the oxygen saturation target of 85% to 92%.

TABLE 3 Proportion of Infants in the Oxygen Saturation Target Range of 85% to 92% at Different Time Points

	3 min	5 min	8 min	10 min
Low-oxygen group	0.06	0.15	0.26	0.38
Moderate-oxygen group	0.18	0.24	0.44	0.38
High-oxygen group	0.11	0.18	0.16	0.13
P	.35	.67	.04	.02

Note that outcomes as 3, 8, and 10 minutes are secondary outcomes and, therefore, must be interpreted with caution. *P* values are for Fisher's tests within each time period. Statistically significant differences were found using Benjamini-Hochberg adjusted pairwise comparisons at 8 minutes for moderate versus high oxygen ($P = .02$), at 10 minutes for low versus high oxygen ($P = .02$), and at 10 minutes for moderate versus high-oxygen ($P = .02$).

guidelines recommended the use of 100% oxygen for the resuscitation of preterm infants.[23] After completion of this study, they were amended to state that, for infants less than 32 weeks' gestation, "blended oxygen and air may be given judiciously."[25] We found that titrating the FIO_2 down from a starting oxygen concentration of 100% was most effective at maintaining infants in a SPO_2 range of 85% to 92% and that these infants spent nearly twice as long in the target SPO_2 range as infants initially resuscitated with 21% oxygen. Furthermore, this approach did not lead to more hyperoxemia compared with initiating resuscitation with room air. Infants in both of these groups were more likely to be in our SPO_2 target range, by 10 minutes of age, than infants resuscitated with a static 100% oxygen concentration.

In a recent study by Vento et al,[13] preterm infants resuscitated with 90% oxygen needed fewer days of mechanical ventilation and oxygen supplementation compared with those resuscitated with 30% oxygen. In our study, intubation rates trended toward being higher in the high-oxygen group (43%) compared with the moderate-oxygen (26%) and low-oxygen groups (29%) as did days on mechanical ventilation, with the mean in the low-oxygen group being 6.9 days compared with a mean of 11.1 days in the high-oxygen group. These finding are consistent with previous studies[4,26] showing that resuscitation with 100% oxygen delayed the onset of spontaneous respirations. Our study was not designed or powered to address these outcomes;

TABLE 4 Oxygen Exposure During Resuscitation

	Low-Oxygen Group	Moderate-Oxygen Group	High-Oxygen Group	*P*
FIO_2 at end of resuscitation, mean (95% CI)	0.36 (0.27–0.45)	0.33 (0.27–0.39)	0.87 (0.77–0.96)	<.001
Infants weaned to 21% oxygen by end of resuscitation, proportion (95% CI)	0.62 (0.44–0.76)	0.56 (0.38–0.74)	0.16 (0.05–0.29)	<.001
Infants maintained in 21% oxygen for ≥1 min before end of resuscitation, proportion (95% CI)	0.32 (0.18–0.47)	0.35 (0.21–0.53)	0.11 (0.03–0.21)	.034
Proportion of resuscitation time with $FIO_2 < 40\%$, proportion (95% CI)	0.58 (0.51–0.66)	0.50 (0.43–0.57)	0.31 (0.24–0.37)	<.001
Duration of resuscitation, mean (95% CI), s	677 (588–766)	665 (549–781)	591 (515–666)	>.05
Total oxygen exposure, mean (95% CI), L of 100% oxygen/kg	28.36 (21.41–35.30)	36.56 (20.11–53.01)	44.98 (32.77–57.19)	.161

Low-oxygen and moderate-oxygen groups were each significantly different from the high-oxygen group ($P < .05$) for FIO_2 at end of resuscitation, proportion weaned to 21% oxygen by the end of resuscitation, proportion maintained in 21% oxygen for 1 minute or longer before end of resuscitation, and proportion of resuscitation time with $FIO_2 < 40\%$. Low-oxygen and moderate-oxygen groups were each significantly different from the high-oxygen group after Bonferroni correction for multiple comparisons ($P < .008$) for FIO_2 at end of resuscitation, proportion weaned to 21% oxygen by the end of resuscitation, and proportion of resuscitation time with $FIO_2 < 40\%$. These results must be interpreted cautiously, because they are not primary outcomes.

TABLE 5 Secondary Outcomes

	Low-Oxygen Group	Moderate-Oxygen Group	High-Oxygen Group	*P*
5-min Apgar score, median (interquartile range)	7 (1.5)	8 (2.0)	8 (2.0)	>.05
SNAPPE-II score, mean (95% CI)	25 (18–32)	20 (13–26)	26 (20–31)	>.05
Intubated in delivery room, *n/N*	10/34	9/34	16/38	>.05
Death, *n/N*	1/34	2/34	1/38	>.05
Duration of mechanical ventilation, mean (95% CI), d	6.9 (2.8–11)	5.5 (1.8–9.1)	11.1 (4.4–17.8)	>.05
Bronchopulmonary dysplasia, *n/N*	18/33	19/32	22/37	>.05
Days in hospital, mean (95% CI)	56 (43–68)	57 (46–67)	68 (55–82)	>.05

hence, these results must be interpreted cautiously.

We designed this study to allow for titration of the FIO_2 because we were concerned that a static concentration of 21% oxygen would not safely support oxygenation in this population. Our protocol for titrating oxygen differed from previous studies that made adjustments to FIO_2 less frequently and some that used heart rate to guide titration of oxygen.[13,15,16] In all studies on this topic to date, infants frequently required an increase in FIO_2.[13–16] We found that differences in the time to reach the target SPO_2 were not significantly different ($P = .056$). However, compared with the high-oxygen group, infants in the low-oxygen group took ~2 minutes longer to reach the target SPO_2 range.

Despite different protocols, 4 randomized control trials, including this study,[13,15,16] report similar FIO_2 values at the end of resuscitation ranging from 30% to 44%. In our study, the low- and moderate-oxygen groups did not differ significantly for the outcomes of FIO_2 at the end of resuscitation, proportion weaned to and maintained at 21% oxygen by the end of resuscitation and proportion of resuscitation time with FIO_2 less than 40%. The mean FIO_2 at the end of resuscitation was 87%, as opposed to 100%, in the high-oxygen group because infants not receiving respiratory support were assumed to be inspiring 21% oxygen.

Infants in the low-oxygen groups were 8 times more likely to meet the criteria for treatment failure than infants in the high-oxygen group. This is consistent with findings reported by Wang et al,[16] where one-third of patients met failure criteria and the remainder failed to achieve an SPO_2 of 70% by 3 minutes of age. In a cohort study by Dawson et al,[14] 97 of 105 infants in the room-air group met the failure criterion, and static concentrations of 21% or 100% oxygen were associated with hypoxia and hyperoxia, respectively. By contrast, Escrig et al[15] reported that a similar proportion of infants from both groups met the failure criterion, 3 of 19 in the 30% oxygen group and 4 of 23 in 90% oxygen group. Differences in failure rates between published studies can likely be explained by varying oxygen-titration protocols and treatment-failure criteria.

To our knowledge, this is the first randomized control trial that collected continuous physiologic data for respiratory interventions to determine if the study groups were treated similarly. We did not observe significant differences in the peak inspiratory pressures delivered during artificial ventilation or in the end-tidal CO_2 values between groups. There was a trend toward higher assisted-ventilation rates (breaths per minute) in the low-oxygen group compared with the other 2 groups. One may speculate this occurred because infants in the low-oxygen group were more likely to appear cyanosed, which may have prompted a higher manual ventilation rate. However, we also note that the end-tidal CO_2 values were not lower in this group, which would be expected with higher minute ventilation. The low end-tidal CO_2 values we observed were likely an artifact of the large dead space (2.5 mls) of the sensor and should be interpreted for the purposes of trending only.

Our study is the first to blind the resuscitation team, health care team, outcome assessor, data collector, and statistician to the intervention.The investigator attending deliveries was not blinded to the intervention. This limitation was necessary to allow for titration of oxygen as per the protocol. Although the investigator was not directly involved in the resuscitation or care of the infant, this is a potential source of bias. It is reassuring that the rate of positive-pressure breaths and the peak inspiratory pressures delivered to the infants did not differ significantly between the 3 groups.

The target SPO_2 range of 85% to 92% used in our study may be too high. We chose a static target SPO_2 range that encompasses values observed in healthy infants from 3 to 10 minutes of age.[18,27,28] In future studies, the process of targeting oxygen saturations observed in healthy infants immediately after birth can be facilitated by using a nomogram, such as the one published by Dawson et al.[27]

As expected, we found a dose-response relationship, with infants in the low- and high-oxygen groups spending the most time with SPO_2 lower than 85% and higher than 92%, respectively. This supports that our protocol, to some extent, separated the 3 treatment groups in terms of exposure to oxygen. Although the measured oxygen exposure was not significantly different between the groups, there was a trend toward increasing

exposure from low- to moderate- to high-oxygen groups, with infants in the high-oxygen group receiving nearly twice as much oxygen as those in the low-oxygen group. The lack of a statistically significant difference for this measure was likely a result of our aggressive oxygen-titration protocol.

CONCLUSIONS

In our study, titrating from an initial oxygen concentration of 100% was more effective than starting with 21% oxygen or giving a static concentration of 100% oxygen for maintaining preterm infants in a target SPO_2 range. However, there is valid concern that exposure to 100% oxygen during resuscitation may cause oxidative injury in preterm infants. We do not recommend using a static concentration of 21% oxygen for preterm resuscitation. This does not preclude starting resuscitation with an intermediate concentration of oxygen if an appropriate oxygen-titration schedule is used in conjunction with SPO_2 monitoring.

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