**Local Guideline: Use of inspired oxygen during neonatal resuscitation**

Term neonates should be resuscitated with room air in nearly all circumstances, while the ideal use of oxygen at the start of and during resuscitation of preterm infants is unknown, particularly for the very preterm population\(^{1,2}\). In infants born at <32 weeks GA, both the NRP textbook\(^{3}\) and ILCOR Guidelines on Neonatal Resuscitation\(^{4}\) do not specify an ideal initial fraction of inspired oxygen (F\(_{2}\)O\(_2\)) but note that it likely should be greater than 0.21 and less than 1.0 based on current evidence.

Given this fact, each institution that performs any resuscitations of preterm infants must decide how they will use oxygen in these situations\(^{5,6}\). The decision should be based on the best available evidence\(^ {7,8}\).

**Recommendations for TOH – General & Civic Campuses:**

Based on a review of the literature (see Appendix), we make the following recommendations around the use of inspired oxygen during neonatal resuscitation:

1. Initial F\(_{2}\)O\(_2\) – based on GA:
   a. F\(_{2}\)O\(_2\) of 30% **in babies ≤28+6 weeks GA**\(^ {9}\).
   b. F\(_{2}\)O\(_2\) of 21% **in babies ≥29+0 weeks GA**\(^ {5}\).

   **NOTE:** For patients with known pre-birth risk factors for poor oxygenation (e.g. oligo or anhydramnios, cyanotic congenital heart disease, hemoglobinopathies, etc.), modify the initial F\(_{2}\)O\(_2\) accordingly\(^ {10}\).

2. Modify F\(_{2}\)O\(_2\) during resuscitation based on a case-by-case approach. For resuscitations where a baby is doing well (i.e. non-extensive resuscitation required with the baby having some respiratory effort, tone, and heart rate), we recommend the following method of oxygen titration:
   a. Titrate the oxygen up or down by 10% approximately every 30-60 seconds based on the heart rate and pulse oximetry\(^ {11,12}\). The saturations to target are the same as those found in the standard “targeted saturations” table from the NRP textbook\(^ {5}\). Note that there may be times where this rate of titration (either up or down) may be deemed too slow.

   b. If saturations are not available, oxygen titration (as per 2a) should be guided by the baby’s heart rate and clinical condition\(^ {3,13}\). Continuous monitoring of the HR by auscultation or a cardiorespiratory monitor, until the pulse oximetry is reading properly, should be considered\(^ {14}\).

   **NOTE:** If bradycardia (HR < 100) persists AND is not improving with your resuscitative measures in an unresponsive, flat infant (i.e. Apgar of 1 or less at 1 minute) for more than 30 seconds, the F\(_{2}\)O\(_2\) should be immediately increased to 100%\(^ {12,13}\).
APPENDIX

On December 21, 2011, a PubMed search was performed as follows: (oxygen AND resuscitation AND premature infant); limits – language: English, ages: all infant: birth-23 months, published in the last 5 years. After reviewing the 102 titles, 23 articles (including 8 reviews) were considered most relevant\(^2,5,6,8-27\). Additional information was also sought from conference proceedings, articles from reference lists\(^1,7,28-31\) and the NRP textbook and articles (AAP and ILCOR versions)\(^3,4,32\).

Redundancy, lack of applicability or outdated information was noted in a majority of the publications from 2009 or earlier. Therefore, some of these references are not cited in this guideline.

Key points from a review of the above literature include:

1. The evidence on this subject for term infants is based on “weak” evidence but allows for an acceptable recommendation\(^4,32\). The evidence is weaker for preterm infants.

2. **Too high an F\(_2\)O\(_2\)** may be toxic due to the formation of oxygen free radicals\(^17\) in combination with a neonate’s diminished antioxidant capabilities\(^14,25\). **Too low an F\(_2\)O\(_2\)** may cause PPHN, HIE, or multisystem organ dysfunction\(^25\).

3. **A high F\(_2\)O\(_2\)** may prolong time to spontaneous crying and breathing, increase O\(_2\) consumption, decrease minute ventilation, cause atelectasis, or decrease cerebral blood flow\(^14,25\).

4. Trials (randomized or quasi-randomized) to date are inadequate due to lack of power to truly determine the effect on major preterm infant morbidities (e.g. CLD, NEC, cerebral white matter injury, etc.), and lack of good quality long term follow-up (of term or preterm infants)\(^25\).

5. Several small RCTs have compared a low versus high F\(_2\)O\(_2\) during resuscitation of preterm infants\(^10-12,24,28,29\).
   a. In one blinded trial (<33 wks GA) that used room air as their low F\(_2\)O\(_2\), all neonates required supplemental oxygen due to either having a HR of <100 for 30 seconds or not reaching the desired saturations of 85-92\%\(^10\). In an unblinded trial (<31 wks GA) that used room air as their low F\(_2\)O\(_2\), all neonates required supplemental oxygen to reach their targeted saturations of 75\% at 3 mins and 85\% at 5 mins\(^24\). A cohort study had similar findings\(^16\).

   b. In 2 trials\(^11,12\) comparing 30\% versus 90\% as a starting F\(_2\)O\(_2\) in ≤28 wk GA infants, desired saturations [75\% at 10 minutes\(^11\) versus 75\% at 5 mins and 85\% at 10 mins\(^12\)] were reached at similar times in both groups. The high oxygen groups had greater exposure to oxygen\(^11\), more signs of oxidative stress, more ventilation days and prolonged oxygen supplementation (even to 28 days)\(^12\).

   c. In the trial (<31 wks GA infants) comparing 50\% and 100\% as a starting F\(_2\)O\(_2\), there were no significant differences in any short term outcomes or signs of oxidative stress\(^28\). In a trial (<35 wks GA infants) comparing 100\% continuously versus 100\% with weaning to keep saturations 90-95\% from one minute of life onward, the lower oxygen group has less signs of oxidative stress\(^29\).
6. Several different methods of oxygen titration were used in the studies:
   a. Titrate the oxygen by 20% every 15 seconds based on pulse oximetry \(^{10;27}\).
   b. Titrate the oxygen by 25% every 30 seconds based on pulse oximetry \(^{24}\).
   c. Titrate the oxygen up or down by 10% every 60-90 seconds based on the heart rate and pulse oximetry \(^{11;12}\).

7. Optimal saturations are not known. Preterm infants take longer to reach saturations of >85% \(^{13;31}\). Dawson et al report on saturation levels that could guide changes in the F\(_2\)O\(_2\) \(^{30}\) and these levels are frequently used (including by the European Resuscitation Council \(^{27}\)). Based on a review of several publications, Finer and Wade recommend \(^{14}\): “initial SpO\(_2\) following delivery can be assumed to be around 50% and increases by ~5 to 6% per min for the very preterm infant. This will result in an SpO\(_2\) of 65 to 70% at 3 min, 75 to 80% at 5 min and 85 to 90% by 7 to 8 min of age (p. S59).” The NRP textbook recommends using their standard “targeted saturations” table \(^3\), though this will likely result in unnecessary oxygen administration \(^{27}\).

8. ILCOR recommends that resuscitation of infants <32 weeks GA should be guided by the use of pulse oximetry with judicious use of blended oxygen and air \(^4\). They recommend starting with room air for term or late preterm (34-36 wk GA) infants \(^4\). The NRP textbook lacks clarity but appears to recommend starting with less than 100% but greater than 21% for preterm babies \(^{3;25}\). They recommend using the same “targeted saturations” table to guide oxygen supplementation during resuscitation for term and preterm infants \(^3;32\).

9. Room air, 100% F\(_2\)O\(_2\), or any percentage in-between may be the best starting point. We do not know. Two large RCTs (with a primary outcome of NDI or mortality at 2 years of age) are underway and will hopefully provide further guidance \(^1\).
Reference List


