Management of Oxygen Saturations in Preterm Infants

NHS University Hospitals of Leicester NHS Trust

Trust ref: C129/2006

1. Introduction and who this guideline applies to:

This guideline is aimed at all Health Care Professionals involved in the care of infants within the Neonatal Service.

Key Points:

1. Large trials have demonstrated the importance of keeping oxygen saturations in preterm infants within defined limits (Appendix)
2. Target ranges for oxygen saturations are based on available evidence.
3. It is extremely important not to allow saturations of preterm babies receiving oxygen to rise inappropriately; as this is likely to cause an increase in the risk of Retinopathy of Prematurity (ROP) and other consequences of oxidative stress.
4. Alternative oxygen saturation targets and limits may be appropriate for certain clinical situations and specific conditions. The decision should be taken at consultant level and documented in the infants notes.

Until 36 weeks corrected age, aim to maintain oxygen saturations in the target range 91 - 96% by setting the alarm limits below:

<36 weeks of gestation and in oxygen:

Lower saturation alarm limit: **90%**
Higher saturation alarm limit: **96%**

>36 weeks of gestation and in oxygen:

Lower saturation alarm limit: **92%**
Higher saturation alarm limit: **98%**

For babies of any gestation being nursed in air, alarm limits may be increased to 100%

2. Evidence summary

Decades of research has been invested in attempting to deliver sufficient tissue oxygenation whilst avoiding potential harmful effects of oxidative stress in preterm infants. A number of randomised trials of oxygen saturation targets have been performed in preterm infants using pulse oximetry. Evidence from these trials forms the basis of the current recommendations.

The Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP) trial demonstrated that an oxygen target of between 96 to 99% (commenced in preterm infants at a mean corrected age of 35 weeks) was associated with greater morbidity (including greater risk of CLD and longer duration of hospitalisation) than a lower target range of 89 to 94% [1].

The Benefits of Oxygen Saturation Targeting trial (BOOST) [2] studied oxygen saturation targets of 91 to 94% versus 95 to 98% in infants born <30 weeks of gestation who remained in oxygen after 3 weeks (32 weeks CGA). Targeting higher oxygen saturations prolonged oxygen use and increased length of hospital stay without any demonstrable improvement in growth or development. A number of compelling contemporaneous cohort studies suggested that lower oxygen saturation targets improved short term outcomes; however, effects on mortality and important longer term outcomes remained unknown.[3,4]

This prompted a number of large international trials, designed with similar protocols (NeOProM Collaborative Group [3]) comparing oxygen saturation targets between a higher oxygen saturation range (91 to 95%) and a lower oxygen saturation range (85 to 89%). Infants were born before 28 weeks' gestation and enrolled within 24 hours of birth. The primary outcome was a composite outcome of death and major disability at two years corrected age. A prospective meta-analysis was planned as part of the collaborative design. The trials included the Canadian Oxygen Trial [COT][5]; Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial [SUPPORT][6]; and Benefits of Oxygen Saturation Targeting trial [BOOST II][7]. During the course of these trials, calibration software was revised because of an anomaly noted in the algorithm used for the pulse oximeters. The results of the meta-analysis (including a total of 4965 infants) were published in a 2017 Cochrane review [8] are summarised below:

Primary outcome:
No significant difference in the composite primary outcome of death or major disability (typical RR 1.04, 95% confidence interval (CI) 0.98 to 1.10; typical RD 0.02, 95% CI -0.01 to 0.05; 5 trials, 4754 infants).

Secondary outcomes:
Targeting the lower oxygen saturation range (below 90%) resulted in:

- A significant increase in death at 18 to 24 months corrected age associated with the lower target range (RR 1.16, 95% CI 1.03 to 1.31)

- A significant increase in necrotising enterocolitis associated with the lower target range (RR 1.24, 95% 1.05 to 1.47)
- A significant decrease in retinopathy of prematurity requiring treatment (typical RR 0.72, 95% CI 0.61 to 0.85)

Other outcomes:
There were no significant differences between the two treatment groups for major disability including blindness, severe hearing loss, cerebral palsy, or other important neonatal morbidities.

When subgroup analyses were performed comparing the original and revised calibration software, a significant difference in the treatment effect between the two groups was seen, with a significantly larger treatment effect seen for those infants using the revised algorithm (death by 18-24 months - typical RR 1.38, 95% CI 1.13 to 1.68; 3 trials, 1716 infants) [8]. Post-hoc unadjusted analysis of the BOOST-II study showed the low oxygen saturation group (85 to 89%) had higher rates of death than the high oxygen saturation group (91 to 95%) (21 versus 18 percent, RR 1.2, 95% CI 1.01-1.43); irrespective of the monitor algorithm[9]. Further post-hoc SUPPORT trial analyses showed SGA infants specifically had the highest mortality. Being most vulnerable to experiencing the lowest median oxygen saturations and more episodes of intermittent hypoxia in the early neonatal period.[10]

Interpreting this into practice:
Current National[11] and International[12] guidelines recommend saturations targets aligned to the higher oxygen saturation range of the NeOProM trials (avoid <90 % and >95%). Recommended alarm limits vary; except in suggesting tight control, minimising fluctuations and an upper limit of 95%.[11-16]

Pulse oximeters estimate arterial oxygen saturations (SaO_2) within limits of accuracy (+/- 3%) that widen as the saturations (SpO_2) fall below 93%.[17] Maintaining a tight oxygen saturation range is challenging;[13-15] adjusting FiO_2 in small increments or decrements can help avoid extreme fluctuations.

Our recommendation for oxygen saturation targeting for preterm infants is detailed in the figure above. Guidance is also given for term-corrected infants, but for those infants with other conditions, such as CLD, pulmonary hypertension and congenital heart disease the required oxygen saturation targets may need to be individualised.

3. Education and Training

None

4. Monitoring Compliance

None

5. Supporting References

1. The STOP-ROP Multicenter Study Group. Supplemental Therapeutic Oxygen for Prethreshold Retinopathy Of Prematurity (STOP-ROP), a Randomized, Controlled trial. I: primary outcomes. Pediatrics 2000;105:295
2. Askie LM, Henderson-Smart DJ, Irwig L, Simpson JM. Oxygen-saturation targets and outcomes in extremely preterm infants. N Engl J Med 2003;349:959
3. Tin W, Milligan WA, Pennefather, Hey E. Pulse oximetry, severe retinopathy, and outcome at one year in babies of less than 28 weeks gestation. Arch Dis Child Fetal Neonatal Ed 2001;84:F106
4. Askie LM, Brocklehurst P, Darlow BA, Finer N, Schmidt B, Tarnow-Mordi W, the NeOProM Collaborative Group. NeOProM: Neonatal Oxygenation Prospective Meta-analysis Collaboration study protocol. BMC Pediatrics 2011; 11:6
5. Schmidt B, Whyte RK, Asztalos EV, et al. Effects of targeting higher vs lower arterial oxygen saturations on death or disability in extremely preterm infants: a randomized clinical trial. JAMA 2013;309:2111
6. SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network, Carlo WA, Finer NN, et al. Target ranges of oxygen saturation in extremely preterm infants. N Engl J Med 2010;362:1959
7. BOOST II United Kingdom Collaborative Group, BOOST II Australia Collaborative Group, BOOST II New Zealand Collaborative Group, et al. Oxygen saturation and outcomes in preterm infants. N Engl J Med 2013; 368:2094
8. Askie LM, Darlow BA, Davis PG, Finer N, Stenson B, Vento M, Whyte R. Effects of targeting lower versus higher arterial oxygenation saturations on death and disability in preterm infants. Cochrane Databse Syst. Rev. 2017 Apr 11;4:CD011190
9. BOOST-II Australia and United Kingdom Collaborative Groups, Tarnow-Mordi W, Stenson B, et al. Outcomes of Two Trials of Oxygen-Saturation Targets in Preterm Infants. N Engl J Med 2016;374:749
10. Di Fiore JM *et al*. Patterns of Oxygenation, Mortality and Growth Status in the Surfactant, Positive Pressure and Oxygen Trial Cohort. J Pediatr 2017;186:49
11. National Institute for Health and Care Excellence. Specialist neonatal respiratory care for babies born preterm. NICE Guideline NG124. April 2019. https://www.nice.org.uk/guidance/ng124 (Guideline and published final evidence reviews B and D accessed June 2020)
12. Sweet DG, *et al.* European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2019 Update. Neonatology 2019;115:432
13. Stensvold HJ, Saugstad OD. The oxygen dilemma: oxygen saturation targets in preterm infants. Acta Pediatrica 2019;108:1156
14. Saugstad OD. Oxygenation of the Immature Infant: A Commentary and Recommendations for Oxygen Saturation Targets and Alarm limits. Neonatology 2018;114:69
15. Van Zanten HA, Pauws SC *et al.* Effect of a smaller range on the compliance in targeting and distribution of oxygen saturation in preterm

infants. Arch Dis Child Fetal Neonatal Ed 2018;103(5):F430
16. Schmidt B, Whyte RK. Oxygen saturation target ranges and alarm settings in the NICU: What have we learnt from the neonatal oxygenation prospective meta-analysis (NeOProM)? Sem Fetal and Neonatal Med 2020;25:101080
17. Rosychuk RJ, Hudson-Mason A *et al.* Discrepancies between Arterial Oxygen Saturation and Functional Oxygen Saturation Measured with Pulse Oximetry in Very Preterm Infants. Neonatology 2012;101:14

With acknowledgement of:
Martin R. (ed Weisman LE, Kim MS). Oxygen monitoring and therapy in the newborn. UpToDate (accessed May 2017 and June 2020).

6. Key Words

Pulse Oximetry, Retinopathy of Prematurity

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS			
Original Author: : Elaine Boyle **Reviewed by:** Farooq Syed **Guideline Lead:** Sumit Mittal			**Executive Lead** Chief Nurse
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
Dec 2010	**1**		Interim Guidance (EMB)
Oct 2015	**2**	Author (EMB) Neonatal Guidelines Meeting Neonatal Governance Meeting	For further review in one year
Jun 2017	**3**	EMB / guidelines lead – REM Neonatal Guidelines Meeting Neonatal Governance Meeting	Information and references updated in line with recent meta- analysis

July 2020	**4**	Neonatal Guidelines Meeting Neonatal Governance Meeting	
Aug – Oct 2023	**5**	Neonatal Guidelines Meeting Neonatal Governance Meeting	No changes made