Newborn Clinical Network

Practice recommendation for Oxygen saturation targets for newborns cared for in neonatal units, New Zealand

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Disclaimer
The content of this practice recommendation does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

Public Domain Notice
This practice recommendation is intended for use by secondary care practitioners involved in the care of newborns requiring oxygen. It provides the best evidence currently available to assist informed decision making by parents/caregivers and their health care providers to improve their health outcomes.

Glossary
ALTE  Apparent Life Threatening Event
ANZNN  Australian and New Zealand Neonatal Network
BOOST  Benefits of Oxygen Saturation Targets
CI  Confidence interval
CLD  Chronic lung disease
NEC  Necrotising enterocolitis
NEJM  New England Journal of Medicine
PPHN  Persistent Pulmonary Hypertension of the Newborn
PMA  Postmenstrual age = gestation + postnatal age in weeks
RCT  Randomised Controlled Trial
ROP  Retinopathy of prematurity
RR  Relative risk
Introduction
Oxygen therapy for preterm and term infants improves survival in situations where lung immaturity, infection or other pulmonary conditions reduce the arterial oxygen concentration. Oxygen saturations provide the best continuous measure of arterial oxygen concentrations and are easily measured.

Several recent randomized controlled trials (RCTs) have suggested that survival may be reduced if the oxygen saturation target is too low. On the other hand retinopathy of prematurity (ROP) is higher when high arterial oxygen concentrations occur, particularly in the early period following extremely preterm birth. These two outcomes require consideration in setting optimal oxygen saturation target levels.

Background
Large RCTs have been published since 2003 comparing higher and lower saturation target ranges with the main outcome measures of survival, chronic lung disease (CLD) and ROP. Growth and development, infection in particular necrotising enterocolitis (NEC) have also been reported.

The BOOST I study (Askie NEJM 2003) compared target saturations of 91-94% compared with 95-98% in infants born <30 weeks who remained dependent on supplemental oxygen at 32 weeks gestation in 358 infants. The higher saturation range conferred no benefit in terms of growth or development, but they were in oxygen for longer duration, higher rates of oxygen requirement at 36 weeks gestation and higher rate of home based oxygen therapy.

Larger multi-centred international collaboration resulted in the BOOST II (NEJM 2013) study which compared the saturation targets of 85-89% or 91-95% in preterm infants born <28 weeks in 3 countries. Key finding of this study was the increased rate of death in the infants in the lower target range (23.1% vs 15.9% RR 1.45, 95%CI 1.15-1.84 P=0.002), but death was not attributable to any single cause. Infants in the lower group had lower rates of treatment of ROP (10.6% vs 13.5%; RR 0.79; 95%CI, 0.63-1.00; P=0.045), and an increased rate of NEC requiring surgery or causing death (10.4% vs 8.0%; RR 1.31; 95%CI, 1.02-1.68; P=0.04). There was heterogeneity for mortality between the original oxygen saturation algorithm and the revised algorithm which resulted in clearer separation of the groups. The peak median saturation for infants receiving supplementary oxygen was 89% vs 92%.

The SUPPORT trial (NEJM 2010) also compared the saturation targets of 85-89% or 91-95% in preterm infants born <28 weeks gestation in Canada. This study also found a lower rate of ROP needing treatment (8.6% vs 17.9%; RR 0.52, 95% CI 0.37-0.73; P<0.001) in the lower saturation group. They also found a higher rate of death before discharge (19.9% vs 16.2% RR 1.27; 95% CI 1.01-1.60 P=0.04) in the lower saturation group, although the combined rate of death or severe ROP was not significantly different and this was their primary outcome. Their median saturations were slightly higher 91% vs 94%. Important to the targeted saturation debate are follow-up studies. The SUPPORT follow-up study (Vaucher NEJM 2012) showed no significant differences of later disabilities between the groups.

The ability to maintain saturations in the intended target range has also been analysed. Too narrow target ranges are more difficult to achieve. Some feel that the level of fluctuation in the saturations is also important in determining outcomes such as CLD and ROP.

Conclusions from international commentary favour the avoidance of targeting an oxygen saturation of less than 90% in infants born less than 28 weeks.
Other sources of guidance on target saturations come from reviews with particular focus on supporting infants needing home oxygen. These recommendations focus largely on ex-pre-terms with CLD as defined as oxygen or respiratory support required at 36 weeks gestation. Conclusion from the British Thoracic Society (2009) and the Thoracic Society of Australian and NZ (2008) support the targeting of saturations of 93% or above.

Below is a brief summary of the consequences of hypoxia and impact of excessive oxygen.

**Consequences of hypoxia**

1. Periodic breathing / Apnoea / ALTE
   - Periodic breathing: Saturations below 90% increase the frequency and level of desaturation seen with periodic breathing and central apnoea
   - Apparent life threatening events: In infants with CLD, saturations < 90% are associated with an increase in ALTE events
   - Sleep associated apnoea may be intermittent and associated with elements of obstruction.
2. Pulmonary hypertension: The precise severity and duration of hypoxaemia needed to cause pulmonary hypertension is not known. Oxygen saturation of 94-95% appears to reduce PPHN
3. Neurodevelopment: In view of the many confounding factors an impact of oxygen saturations on neurodevelopment is uncertain
4. Growth: There is evidence to suggest that saturations below 92% may be associated with suboptimal growth in infants with CLD. Improved oxygen saturation may reduce the work of breathing and reduce energy consumption

**Consequences of excess oxygen**

1. Retinopathy: The impact of unmonitored inspired oxygen therapy on the developing retina leading to retinopathy of prematurity is well known
   - After 36 weeks in infants with significant ROP, less laser ablative therapy was needed when targeting saturations 95-98% (BOOST)
2. Pulmonary: Oxidative stress may also impact on the developing and healing lung
   - Higher rates of pneumonia and exacerbations of CLD were seen in the STOP ROP trial (2000) which targeted saturations of 96-99%

**Purpose of these recommendations**

- To standardize the oxygen saturation targets in all neonatal units in New Zealand.
- To facilitate the seamless care for newborns who move between level 2 and level 3 units.
- To provide guidance for weaning oxygen in preterm infants with Chronic Lung Disease or other conditions requiring oxygen at discharge from neonatal units.

**Recommendations**

1. Oxygen saturation monitoring should occur continuously in all newborns who have respiratory distress, or commence oxygen.

   The lowest oxygen saturation level recommended to commence oxygen therapy:
   a) Preterm infants born before 36 weeks gestation should commence oxygen when saturations fall below 90% in room air
   b) Preterm infants once they reach 36 weeks follow the targets for PMA 36 weeks or above
   c) Newborns born at 36 weeks gestation or older should commence oxygen when saturations fall below 93% in room air
2. Target oxygen saturations and alarm limits for babies needing supplemental oxygen

<table>
<thead>
<tr>
<th>Postmenstrual Age</th>
<th>Target saturations</th>
<th>Monitor alarm limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;36 weeks</td>
<td>90-94</td>
<td>89-95</td>
</tr>
<tr>
<td>36 weeks and more</td>
<td>93-97</td>
<td>PPHN 95 and above</td>
</tr>
</tbody>
</table>

3. For babies requiring prolonged oxygen to maintain saturations detailed monitoring with pulse oximetry for 12-24 hours is suggested in the following situations:
   a) Preterm infants <30 weeks at 36 weeks gestation or on being weaned from oxygen
   b) Very preterm infants who meet the criteria for CLD – oxygen dependent at 36 weeks gestation. In the future this may include a standardised test for oxygen requirement which is being developed by ANZNN.
   c) Neonates with meconium aspiration, pulmonary hypoplasia and conditions associated with this e.g. congenital diaphragmatic hernia

Parameters suggested (Thorax 2009, Pretto 2014)
   a) The mean saturation in this preterm group should be >93%
   b) Saturations can be <90% for up to 5% of the 24 hour period

Management and follow-up
   a) Discharge is suggested on low flow oxygen once this is less than 0.5L/min
   b) Assessment and assessment of the ongoing need for this should occur in the first week at home, then every 2-4 weeks
   c) Oxygen reductions should be based on being above minimum criteria, and can usually be reduced down to 0.1L/min or 0.125L/min (depending on flow meter) by 0.05l/min increments
   d) Infants with CLD often require weaning in increments of 0.02L/min down to 0.02L/min where low low flow meters are available
   e) (domiciliary oxygen) Low flow units lowest setting is 0.125L/min in some locations in New Zealand.

For more details on weaning refer to the Starship Oximetry guidelines and the Newborn guidelines; Care of Babies on Oxygen At Home Following Discharge from NICU.
References

BOOST I: Askie LM, Henderson-Smart DJ, Irwig L, Simpson JM. Oxygen saturation targets and outcomes in extremely preterm infants. NEJM 2003; 349:959-967

Oxygen saturation and outcomes in preterm infants. The BOOST II UK, Australia, NZ collaboration NEJM 2013 May 30; 368:2094-2104

SUPPORT: Target ranges of oxygen saturation in extremely preterm infants. NEJM 2010; 362:1959-69


Starship Newborn Services Clinical Guideline: Care of Babies on Oxygen At Home Following Discharge From NICU. September 2010