Oxygen Therapy

Introduction:

Oxygen administration is a common therapy in neonatal nurseries. Despite its documented use in infants for over 75 years,1 Until recently, there were few randomised controlled trials on the most appropriate ranges to maintain oxygen levels for either term or preterm infants, or a threshold value below which oxygen should be administered.2 A wide variation in practice can be seen in terms of modes of administration, monitoring, blood levels, and target ranges for both short and long term oxygen therapy amongst clinicians.3 The recommendations to follow are heavily based on recent RCTs of oxygen saturation targeting.17, 67, 68, 69

Incidence and risk factors:

Each year over 5,000 infants (~ 2% of all infants born) in Australasia receive oxygen therapy during their initial stay in a neonatal nursery and almost 300 of these infants required continued oxygen therapy at home after discharge.4 The incidence of oxygen therapy is dependent on gestational age at birth with 97% of ≤ 27 weekers receiving supplemental oxygen, whilst 79% of 28-31 weekers receive oxygen therapy during their initial hospitalisation.4 Similarly the incidence of chronic lung disease (supplemental oxygen and/or assisted ventilation at 36 weeks pma) drops from 41% in infants born at <27 weeks to 10% for those born at 28-31 weeks.4

The major risk factor for receiving oxygen therapy is extreme prematurity,4 whilst risk factors for prolonged supplemental oxygen (i.e. CLD) include assisted ventilation,5 lack of antenatal steroids,6 and other antenatal risk factors such as maternal ureaplasma infection (see also chronic lung disease guideline - incidence and prevention sections).

Consequences:

What are the effects of too much or too little oxygen?

The effects of adopting a restricted or low oxygen target range include: In the very early neonatal period (<48 hours age): increases mortality and spastic diplegia 8-11, 17, 69 (retrospective observational studies, RCTs); may decrease incidence of severe ROP 12, 70 (observational study, meta-analysis of cohort+RCT studies). > 48 hours age: no difference in early or late mortality, 13-16, 67 ROP progression, 17, 67 sleep architecture 18 or cerebral palsy 16 (RCT, cohort studies); decreases incidence of severe ROP and blindness 19-23 (RCTs), apnea, 24-27 cyanosis and asphyxia 28 (observational studies).

The effects of adopting an unrestricted or high oxygen target range include:

In the early neonatal period (> 48 hours age): increases incidence of severe ROP and blindness 19-23 (RCTs).

In the late neonatal period: no difference in ROP progression 17, 67 or cerebral palsy 16, 67 (RCT); increases chronic lung disease, home oxygen rates, length of hospital stay, rehospitalisation rates 17, 67 (2o outcomes in RCT); decreases short term growth, 16 sleep desaturations, 29 and pulmonary hypertension 30-32 (cohort studies); has no effect on growth and development at 12 months of age (RCT). 67
Diagnosis:

What are the advantages, disadvantages and diagnostic accuracy of different types of oxygen monitoring? Have any clinical outcomes improved as a result of their use?

Blood gases (arterial or capillary) - Because PaO₂ in the newborn is quite labile, intermittent measures such as arterial partial pressure readings from either an indwelling catheters or stab samples, or arterialised capillary PO₂ measures may not reflect an infant’s steady state. There have been no controlled studies that have formally tested the diagnostic accuracy of this type of oxygen monitoring in a neonatal population.

Transcutaneous oxygen monitoring (see also small baby guideline) -

The sensitivity and specificity of detecting hypoxia (PaO₂ <50mmHg) and hyperoxia (PaO₂ > 80-100mmHg) using transcutaneous monitors has been estimated at 83% and 98%, and 87% and 90% respectively. The effect of continuous transcutaneous monitoring on the incidence of ROP has had varying results. Some non-randomised studies have claimed a near abolition of ROP using TcPO₂ monitoring whilst others have reported no difference in the incidence or severity of ROP attributable to TcPO₂ monitoring. The only randomised trial to date examining the effect of transcutaneous monitoring on ROP incidence suggested a modest improvement in ROP rates for infants >1000g BW, but no effect on smaller infants in whom ROP occurs more frequently and is more severe. Conversely there was a trend to higher mortality in the group receiving continuous transcutaneous monitoring.

Pulse oximetry:

Oxygen saturation monitoring using pulse oximetry has the advantages of ease of use and lack of heat related side effects, particularly in extremely preterm infants with sensitive skin. The evidence from non-randomised studies suggests that pulse oximetry is a reliable measure of oxygenation in infants with chronic lung disease and prolonged oxygen dependency, particularly at lower PaO₂ levels. A randomised trial of pulse oximetry monitoring in infants was performed in patients undergoing surgery. This study suggested the value of pulse oximetry in detecting major hypoxic events in anaesthetised children. In the neonate it would appear that a lower alarm limit of 85-90% would optimise the accurate detection of hypoxaemia. The ability of pulse oximeters to reliably detect hyperoxia is however, limited. Studies that have attempted to evaluate the sensitivity and specificity of pulse oximetry in detecting hyperoxia (PaO₂ >90mmHg) have indicated that in order to achieve high sensitivity (>94%) in detecting hyperoxic episodes, low specificity (38-57%) must be accepted. This may result in a high frequency of false alarms in order to reliably detect hyperoxia using pulse oximetry.

Targeted pulse oximetry:

Recent randomised controlled trials (STOP-ROP & BOOST) have compared targeting either standard (89 - 95%) vs high (94 - 99%) saturation in infants with continuing oxygen requirement or respiratory support. These have shown worse short-term pulmonary outcomes, no significant growth and development differences at 12 months, and a non significant trend to less severe retinopathy of prematurity in the high saturation targeted group. Other randomised controlled trials have examined targeting standard (91 - 95%) vs lower (85-89%) saturation from early postnatal life. The NeOProm group of trials consisting of SUPPORT in the US, BOOST 2 in Australia, New Zealand and the UK, and COT in Canada have similar protocols. The SUPPORT trial has reported results showing a decrease in severe retinopathy in survivors however an increase in mortality in the lower saturation targeted group. The BOOST 2 trials have preliminarily reported a similar increase in mortality in the lower targeted group following an improvement in the algorithm to separate the randomised groups. The following recommendations are based on these combined results however it should be noted that the primary outcomes of these trials ie. death or major disability at 18 months - 2 years will not be known until 2014.
Guideline:

Preterm infants:

Resuscitation:

In infants born < 32 weeks evidence supports using blended oxygen commencing at 30% rather than 100% O2 or room air. 74,75,76,77

Pre-ductal saturation is targeted to 90-95% by 10 minutes. 17,76

Early management (all gestations):

Infants < 27 weeks - see also small baby guideline

Pulse oximeters (functional saturation algorithm) are exclusively used to continuously monitor oxygenation during the first 14 days after birth with the alarms set at 88-96% - target range 90-95%. Frequent micro arterial blood gas analysis.

TCMs are not routinely used during the first 14 days after birth. TCMs if used after 14 days correlate best with arterial blood gases when applied to anterior thigh.

Infants ≥ 27 weeks:

Pulse oximeters are used to continuously monitor oxygenation whilst the infant is in oxygen, with the alarms set at 88-96% - target range 90-95%.

Late management (all gestations):

After 1 week of age, infants who are stable or off the ventilator may be monitored by pulse oximetry monitoring with the alarms set at 88-96% - target range 90-95%. The upper alarm limit should only be increased if the infant is in air.

Term infants:

Points to consider:

1. Use of TCMs and pulse oximeters.

2. Targeting oxygen to avoid hypoxia – if pulmonary hypertension not suspected; PaO₂ 60-90mmHg on TCM or ABG; SpO₂ > 95%

3. Targeting oxygen to avoid hypoxia – if severe pulmonary hypertension is suspected - see PPHN guideline; PaO₂ > 80-100 mmHg on TCM or ABG 72,73,78, SpO₂ > 97%

Key points

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<td>Oxygen therapy should be targeted to levels appropriate to the condition, gestational age and postnatal age of the infant. 28</td>
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<tr>
<td>Early saturation targeting in preterm infants in oxygen should aim for SpO₂ 90-95% rather than lower to decrease mortality. 68,69</td>
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<tr>
<td>Late oxygen targeting in preterm infants (usually with CLD) should be aimed at SpO₂ 90-95% range to maximise benefits whilst minimising harms. 17,67</td>
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Initial resuscitation in infants < 32 weeks should commence with 30% oxygen \(^{74,75,76,77}\) \(1b / A\)

Term infants with severe PPHN may benefit from targeting higher oxygen levels (saturations ≥ 97% and PaO\(_2\) 80 - 100 mmHg) \(^{72,73,78}\) \(5 / D\)

**References**

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13. Askie LM, Henderson-Smart DJ. Restricted versus liberal oxygen exposure for preventing morbidity and mortality in preterm or low birth weight infants. Cochrane Database of Systematic Reviews, 2000; Issue 1
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