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Oxygen Saturation Targets for Preterm Infants Clinical Pathway

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Updated: March 9, 2023

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Rationale

This clinical pathway was developed by a consensus group to standardize the target oxygen saturation range for preterm infants <35 weeks gestation requiring respiratory support. It addresses the following clinical problems:

1. Target oxygen saturation range
2. Pulse oximetry alarm limits
3. Histogram analysis

Background

The use of supplemental oxygen plays a critical role in the care of premature infants, but unrestricted use can also lead to unintended harm. Hyperoxia (>95% SpO2) contributes to retinopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD), while hypoxia (<90% SpO2) is associated with increased mortality and necrotizing enterocolitis (NEC). Combined data from large, randomized control trials have indicated that infants with a targeted oxygen saturation range of 90-95% have decreased rate of mortality compared to an oxygen range of 85-89% (1-6). Adherence to intended target saturations in preterm infants is low and improving compliance is difficult (7-9). The use of histogram analysis is emerging as a clinical decision-making aid and an objective way to measure oxygen saturation trends over a period of time. Use of histograms by the clinical team may improve time at goal saturations, decrease rate and/or severity of comorbidities and identify infants in need of respiratory support adjustments (10-14).

Published Data / Level of Evidence

I. Oxygen Trials
   a. The first published randomized controlled trial (RCT) of differential targeting of oxygen saturations was the Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP) trial, published in 2000 (1)
      i. An oxygen target goal of SpO_2 between 96 to 99% in preterm infants was associated with greater risk of BPD and longer duration of hospitalization than those assigned to a lower target range of 89 to 94 percent
   b. A second RCT that randomized infants to treatment at a later postnatal age was the BOOST (Benefits of Oxygen Saturation Targeting) trial (N = 358 infants), which hypothesized that maintaining higher oxygen saturation target ranges (95%–98% vs 93%–96%) would improve growth and neurodevelopmental outcomes (2)
      i. The study reported no benefit to the higher saturation range but did find, similar to the STOP-ROP trial, that infants in the high-saturation arm had significant increases in BPD, length of oxygen therapy and home oxygen
   c. In 2003, an international meeting of experts planned to harmonize five RCTs with similar populations of extremely premature infants in order to conduct a prospective metanalyses after completion of the individual trials. They compared the same pulse oximeter saturation (SpO2) target range and used identically modified study oximeters to make the group allocation.
      i. Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) (3)
         1. Infants treated with the use of an oxygen-saturation target of 85 to 89%, as compared with a target of 91 to 95%, had decreased rates of ROP (8.6% vs. 17.9%, P<0.001) but increased rates of death (19.9% vs. 16.2%, P=0.045)
      ii. Benefits of Oxygen Saturation Targeting II (BOOST II) UK, AUS, and NZ (4)
         1. The rate of death was significantly higher in the lower-target group than in the higher-target group (23.1% vs. 15.9%; P=0.002).
         2. Infants in the lower-target group for oxygen saturation had a reduced rate of ROP (10.6% vs. 13.5% ;P=0.045) and an increased rate of NEC (10.4% vs. 8.0%; P=0.04)
      iii. Canadian Oxygen Trial (COT) (5)
         1. Targeting oxygen saturations of 85% to 89% compared with 91% to 95% had no effect on death or disability at 18 months.
      iv. Neonatal Oxygenation Prospective Meta-analysis (NeOProM) (6)
         1. Combined the individual participant data of 4965 extremely premature infants that had been randomly assigned to arterial oxygen saturations of 85-89% or 91-95%
         2. The primary outcome of death or disability at 18 to 24 months did not differ significantly between the groups
         3. Significant increase in mortality before hospital discharge and NEC was found in the restricted oxygen group

II. Adherence to Oxygen Target Goals

a. Compliance in targeting oxygen therapy in preterm infants varies substantially between centers but overall adherence is low, especially when maintaining the SpO2 below the upper limit (7-9)
b. Presence of a policy of setting oximeter alarms at the target range limits was associated with improved target range compliance (7)
c. Prolonged hyperoxia has been associated with increase patient to nurse ratios (8)
d. Manual documentation of hyperoxemic and hypoxemic episodes results in significant underreporting of such events (9)

III. Histogram Analysis

a. Histogram analysis from patient monitors is an easy and objective way off quantifying oxygen saturation trends. The numerical and graphical representation allows clinicians to easily observe a change in pattern over time.
b. Histogram monitoring improved time at goal saturations and was associated with a reduction in death or severe retinopathy of prematurity (ROP) (10)
c. Histogram aids in early identification of infants at risk for prolonged respiratory support, while median SpO2 does not (11)
d. Histogram analysis is a tool that can help predict need for escalation of respiratory support and readiness for transition from respiratory support (12-14)

Clinical Management

This pathway incudes any neonate with gestational age at birth <35 weeks, requiring supplemental oxygen. It excludes infants with cyanotic congenital heart disease, acute pulmonary hypertension or otherwise specified by neonatologist order.

Target Oxygen Saturation	a. Oxygen saturation target is between 90-95% b. Maintain target until oxygen supplementation is discontinued
Alarm Limits	a. High alarm limit on monitor set at 95% and low alarm limit set at 90% b. Correct alarm limits should be confirmed by bedside RN at the start of each shift
Histogram Analysis	a. Providers are encouraged to review histograms on all premature infants requiring oxygen at least once per day b. Bedside RN should be referencing the histogram periodically to assist in oxygen titration. If the histogram is consistently showing SpO2 out of range more than 50% of the time, the RN needs to contact the provider c. Goal to be in target oxygen saturation range 80% of the time

Summary

The ideal target oxygen range is a compromise among negative outcomes associated with either hyperoxemia (e.g. ROP, BPD) or hypoxemia (e.g. NEC, death). Recent RCTs suggest that a targeted oxygen saturation range of 90% to 95% may be safer than 85% to 89%. Adhering to this narrow target range is challenging but utilizing alarm limits and histogram analysis can improve the time an infant spends in target range and subsequently decrease associated negative outcomes.

Glossary

- Extremely Premature Infant – defined as <28 weeks gestation
- BPD – Bronchopulmonary Dysplasia
- NEC – Necrotizing Enterocolitis
- ROP- Retinopathy of Prematurity
- SpO2 – Pulse Oxygen Saturation
- RCT – Randomized Control Trial

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Outcome Measures

1. Percent of time spent in target oxygen saturation range
2. Percent of time alarm limits are correct on monitor

Clinical Pathway Team

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Date Approved by JHACH Clinical Practice Council:

Date Available on Webpage: 06/14/2023

Last Revised: 03/09/2023

Last Formatted: 03/09/2023

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