WHO recommendation on oxygen therapy for preterm newborns

17 November 2015

Recommendation

During ventilation of preterm babies born at or before 32 weeks of gestation, it is recommended to start oxygen therapy with 30% oxygen or air (if blended oxygen is not available), rather than with 100% oxygen.

The use of progressively higher concentrations of oxygen should only be considered for newborns undergoing oxygen therapy if their heart rate is less than 60 beats per minute after 30 seconds of adequate ventilation with 30% oxygen or air.

(Strong recommendation based on very low-quality evidence)

Publication history

First published: November 2015

Updated: No update planned

Assessed as up-to-date: November 2015

Remarks

- These recommendations are the same as those in the WHO guidelines on basic newborn resuscitation
- Oxygen concentration should be guided by blood oxygen saturation levels. However, measurement of these saturation levels should not supersede early efforts at resuscitation of the preterm newborn and hence saturation-level monitoring should be initiated 2 minutes after birth.
- The target oxygen saturation levels are as follows:

<table>
<thead>
<tr>
<th>Time (after birth)</th>
<th>All preterm infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 minutes</td>
<td>55% – 75%</td>
</tr>
<tr>
<td>3 minutes</td>
<td>65% – 80%</td>
</tr>
<tr>
<td>4 minutes</td>
<td>70% – 85%</td>
</tr>
<tr>
<td>5 minutes</td>
<td>80% – 90%</td>
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</tbody>
</table>
The adjustment of the concentration of oxygen levels should be by 10% (FiO2=0.1) per 30 seconds and must be guided by oxygen saturation levels reached.

**Background**

Preterm birth, defined as birth before 37 weeks of gestation, is the single most important determinant of adverse infant outcomes, in terms of survival and quality of life. (1) Globally, it is the leading cause of perinatal and neonatal mortality and morbidity. (2) Preterm infants are particularly vulnerable to complications due to impaired respiration, difficulty in feeding, poor body temperature regulation and high risk of infection. (3-5) With the increasing contribution of neonatal deaths to overall child mortality, it is critical to address the determinants of poor outcomes related to preterm birth to achieve further reductions in child mortality. (6-8)

Infant mortality and morbidity from preterm birth can be reduced through interventions delivered to the mother before or during pregnancy, and to the preterm infant after birth. (9) Interventions can be directed at all women for primary prevention and reduction of the risk of preterm birth (e.g. smoking cessation programme) or aimed at minimizing the risk in women with known risk factors (e.g. pregestational agents, cervical cerclage). (10) However, the most beneficial set of maternal interventions are those that are aimed at improving outcomes for preterm infants when preterm birth is inevitable (e.g. antenatal corticosteroids, magnesium sulfate and antibiotic prophylaxis). (9) Special care of the preterm newborn to prevent and treat complications of prematurity is also critical to newborn survival. In high-income countries, reductions in mortality rates in infants that were born preterm have been driven largely by improved care and, more importantly, by appropriate policy changes.

**Methods**

The recommendations were developed using standard operating procedures in accordance with the process described in the WHO handbook for guideline development (11). Briefly, these included (i) identification of priority questions and critical outcomes, (ii) retrieval of the evidence, (iii) assessment and synthesis of evidence, (iv) formulation of recommendations, and (v) planning for the dissemination, implementation, impact evaluation and updating of the guideline.

The scientific evidence underpinning the recommendations was synthesized using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (12). Up-to-date systematic reviews were used to prepare evidence profiles for the priority questions. WHO then convened a Technical Consultation in May 2014 where an international group of experts – the Guideline Development Group (GDG) – formulated and approved the recommendations based on the evidence profiles.

In November 2014, an online consultation of the GDG was conducted to review and revise the recommendations in the light of the findings of a large implementation trial of antenatal corticosteroids in low-resource countries.

Further information on procedures for developing this recommendation are available [here](#).
**Recommendation question**

For this recommendation, we aimed to answer the following question:

- In newly born preterm babies born before 32 weeks of gestation (P), is optimal oxygen therapy (O), compared to no guided administration (C), effective in improving newborn outcomes (O)? if so:
  - What concentration of oxygen should be administered?
  - What should guide the administration of the oxygen to these babies?

**Evidence summary**

*Lower oxygen concentration (room air to ? 50%) versus higher oxygen concentrations (> 50%) for positive pressure ventilation (PPV) of preterm neonates at birth*

Evidence related to the starting and progression of oxygen concentration during ventilation was extracted from a systematic review of six RCTs involving 484 newborns. (13).

An updated literature search did not identify any additional eligible studies. Five of the included trials were conducted among neonates born at a gestational age less than 32 weeks in HICs. The sixth was a multicentre trial that was conducted among preterm and term neonates in high- and low-income countries. Most of the studies had serious methodological limitations that affected the overall quality of the evidence. Low oxygen concentration was defined as receiving room air (21% oxygen concentration, 4 studies), 30% (1 study) or 50% (1 study) oxygen concentration. High oxygen concentration was defined as receiving 100% (4 studies), 90% (1 study) or 80% (1 study) oxygen concentration.

**Neonatal death:** There was significant benefit of using low oxygen concentrations for resuscitation in terms of overall and in-hospital neonatal mortality: eight trials demonstrated that the use of low oxygen concentration or air for preterm babies resuscitated with PPV immediately after birth was associated with a 37% lower risk of overall or in-hospital mortality (RR 0.63, 95% CI 0.44–0.92).

**Severe neonatal morbidity:** There was no association between ventilation with low oxygen concentrations for neonatal resuscitation and severe morbidities, including BPD, retinopathy of prematurity, NEC, severe IVH, the proportion of infants reaching target oxygen saturation by 10 minutes after birth, the duration (in days) of mechanical ventilation or the need for endotracheal intubation during resuscitation.

**Subgroup analysis (preterm babies born at 32–36 weeks versus < 32 weeks of gestation)**

Except for two of the studies – Saugstad et al. (14) and Kapadia et al. (15) – all other studies in the review enrolled preterm babies born before 32 weeks of gestation. Saugstad et al. included both term and preterm neonates, with approximately 95% of enrolled neonates being born at 32 weeks or later. For the purpose of this review, the results of the study were stratified into those born at 32–36 weeks and those born before 32 weeks, and low versus high oxygen concentrations were compared. Kapadia et al. enrolled preterm infants born before 35 weeks of gestation (the mean gestation being 30 weeks) but was excluded because of non-availability of data for the two subgroups of interest.

**Preterm babies born at 32–36 weeks of gestation:** There was a 42% lower risk of in-hospital mortality observed in the lower oxygen concentration group compared to the higher oxygen concentration group (RR 0.58, 95% CI 0.34–0.97). No morbidity outcomes were available from the Saugstad et al. study.

**Preterm babies born at < 32 weeks of gestation:** There was inconclusive evidence regarding the risk of
mortality (RR 0.69, 95% CI 0.39–1.22) and the same was true for all the critical outcomes, including BPD, NEC, IVH, retinopathy of prematurity (ROP), and the proportion reaching target saturation by 5 or 10 minutes after birth.

Further information and considerations related to this recommendation can be found in the WHO guidelines, available at:

http://apps.who.int/iris/bitstream/handle/10665/183037/9789241508988_eng.pdf?sequence=1
http://apps.who.int/iris/bitstream/handle/10665/183038/WHO_RHR_15.17_eng.pdf?sequence=1

Implementation considerations

- The successful introduction of this recommendation into national programmes and health-care services depends on well-planned and participatory consensus-driven processes of adaptation and implementation. The adaptation and implementation processes may include the development or revision of existing national guidelines or protocols based on this recommendation.
- The recommendation should be adapted into a locally appropriate document that can meet the specific needs of each country and health service. Any changes should be made in an explicit and transparent manner.
- A set of interventions should be established to ensure that an enabling environment is created for the use of the recommendations, and that the behaviour of the healthcare practitioner changes towards the use of this evidence-based practice.
- In this process, the role of local professional societies is important and an all-inclusive and participatory process should be encouraged.

Research implications

The GDG did not identify any high-priority question related to this recommendation.

Related links


Supporting systematic reviews:


Other links of interest

Managing Complications in Pregnancy and Childbirth: A guide for midwives and doctors
References
