WHO recommendation on continuous positive airway pressure therapy for the treatment of preterm newborns with respiratory distress syndrome

17 November 2015

Recommendation

Continuous positive airway pressure therapy is recommended for the treatment of preterm newborns with respiratory distress syndrome.

(Strong recommendation based on low-quality evidence)

Publication history

First published: November 2015

Updated: No update planned

Assessed as up-to-date: November 2015

Remarks

- The GDG felt strongly that the technological context of care, including the ability to monitor oxygen saturation and cardiorespiratory status, must be considered prior to instituting any respiratory intervention (supplemental oxygen, continuous positive airway pressure [CPAP] or ventilator support) to critically ill neonates in less-developed medical settings, as these interventions have the potential to lead to more harm than benefit.
- This recommendation should be implemented in health-care facilities that can provide quality supportive care to newborns. If oxygen therapy is to be delivered with CPAP, low concentrations of blended oxygen should be used and titrated upwards to maintain targeted blood oxygen saturation levels.
- Where blenders are not available, air should be used; 100% oxygen should never be used because of demonstrable harms. Respiratory distress syndrome can be diagnosed on the basis of clinical or radiological criteria.
**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. progestational 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 with or at risk of respiratory distress syndrome (P), is continuous positive airway pressure (I), compared with routine care (C), effective in preventing adverse newborn outcomes? If so:
Under what conditions and when should continuous positive airway pressure be provided? What are the indications for additional interventions?

Evidence summary

Any continuous positive airway pressure (CPAP) therapy versus oxygen therapy by head box, facemask or nasal cannula for respiratory distress syndrome (RDS) in preterm newborns.

Evidence for this recommendation was extracted from a Cochrane review (13). An updated literature search in May 2014 found no additional relevant studies. The review included six trials from HICs, five of which were randomized trials and one quasi-randomized. The trials enrolled preterm babies with radiological or clinical features of RDS, and the interventions included continuous distending pressure (CDP), CPAP using nasal prongs, nasopharyngeal/endotracheal tubes or continuous negative pressure. These were compared with oxygen delivered by head box, facemask or nasal cannula. Antenatal corticosteroids were additionally used in two of the trials and surfactants were used in one.

**Neonatal death:** Compared to the comparison arm, CPAP was associated with a 48% reduction in overall in-hospital neonatal mortality (17.9% versus 9.1%; RR 0.52, 95% CI 0.32–0.87; 6 studies, 355 preterm babies). There was also a 35% reduction in the risk of the combined outcome of death or the need for assisted ventilation in preterm babies with RDS (RR 0.65, 95% CI 0.52–0.81). Subgroup analysis by gestational age (28–32 weeks and 32–36 weeks) showed no significant differences in RDS-specific in-hospital mortality.

**Severe neonatal morbidity:** CPAP, as compared to oxygen therapy, was associated with a significantly lower risk of respiratory failure requiring assisted ventilation, but was also associated with a higher risk of pneumothorax and air leaks. In five trials with 314 preterm neonates, respiratory failure requiring assisted ventilation occurred in 36.4% on CPAP compared to 52.5% on oxygen therapy (RR 0.72, 95% CI 0.56–0.91). However, the risk of pneumothorax in the CPAP-treated neonates increased more than two-fold (RR 2.64, 95% CI 1.39–5.04). Similarly, the risk of air leaks was also increased among preterm neonates on CPAP (14.5% versus 6.1% in controls; RR 2.42, 95% CI 1.26–4.65). There was no evidence of significant differences between the groups treated with CPAP or standard oxygen therapy in terms of the need for surfactant therapy (RR 0.43, 95% CI 0.12–1.48) or BPD (RR 1.22, 95% CI 0.44–3.39; 3 studies, 260 preterm neonates).

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 identified that further research on the following high-priority questions is needed:

- What is the best modality for providing CPAP? e.g. nasal intermittent positive pressure ventilation, nasal flow cannulas, etc.
- What is the role of CPAP for babies with apnoea of prematurity that persists despite giving methylxanthines/caffeine?
- What is the efficacy of surfactants in a context where antenatal corticosteroids and early CPAP is provided (without immediate obligatory mechanical ventilation) for babies who are at risk of respiratory distress syndrome (e.g. InSURE – intubation, surfactant replacement therapy and extubation)?

Related links


Supporting systematic reviews:

Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants

Other links of interest

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

Pregnancy, Childbirth, Postpartum and Newborn Care: A guide for essential practice

WHO Programmes: Sexual and Reproductive health

Maternal Health

Infant, Newborn Health

References

2. Kinney MV, Lawn JE, Howson CP, Belizan J. 15 million preterm births annually: what has changed
13. †Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. Cochrane


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