WHO recommendation on the early administration of surfactant in intubated preterm newborns with respiratory distress syndrome

17 November 2015

Recommendation

In intubated preterm newborns with respiratory distress syndrome, surfactant should be administered early (within the first 2 hours after birth) rather than waiting for the symptoms to worsen before giving rescue therapy.

(Conditional recommendation [only in health-care facilities where intubation, ventilator care, blood gas analysis, newborn nursing care and monitoring are available] based on low-quality evidence).

Publication history

First published: November 2015

Updated: No update planned

Assessed as up-to-date: November 2015

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 who have or are at risk of respiratory distress syndrome (P), is surfactant therapy (I), compared with routine care without surfactants (C), effective in reducing adverse newborn outcomes (O)? If so:
  - How early should the surfactant therapy be started?
  - Should surfactants be given for prophylaxis in newborns where respiratory distress syndrome has not yet set in, or selectively when existing respiratory distress is worsening?
  - Which types of surfactant are effective – animal-derived or synthetic; protein-containing or protein-free?

**Evidence summary**

*Early (within the first 2 hours after birth) versus delayed selective surfactant therapy (given after 2 hours with worsening RDS) for preterm neonates intubated for clinically or radiologically established RDS*

Evidence for this recommendation was extracted from a Cochrane review that evaluated the effects of early surfactant administration (within the first 2 hours of birth) for preterm newborns intubated for radiological and/or clinical features of RDS requiring assisted ventilation (13).

The comparison group had delayed selective surfactant therapy administered only when they developed
established RDS. The review included six studies – five from HICs and one from Brazil. Four studies used animal-derived surfactants and the other two used a synthetic surfactant. An updated search for the Cochrane review did not find any additional studies that met the eligibility criteria.

Neonatal death: In six trials (3577 babies), early surfactant administration within the first 2 hours of birth for preterm newborns intubated for RDS was associated with lower risk of overall and in-hospital neonatal mortality compared to controls (RR 0.84; 95% CI 0.74–0.95; RR 0.88; 95% CI 0.78–0.99, respectively). There was inconclusive evidence on mortality risk with early surfactant administration compared with delayed therapy in the only study conducted in an LMIC (RR 0.76, 95% CI 0.46–1.26; 75 neonates).

Severe neonatal morbidity: Early surfactant administration was associated with a lower risk of BPD (RR 0.67, 95% CI 0.54–0.84; 4 studies, 3082 neonates) and air leaks (RR 0.64, 95% CI 0.48–0.78; 2 studies, 463 neonates). No association was observed in the risk of severe IVH or confirmed bacterial sepsis, which were only reported in the single study from Brazil (14).

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 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

WHO recommendations on interventions to improve preterm birth outcomes (2015) — full document and evidence tables

Supporting systematic reviews:


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


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