

Early surfactant for respiratory distress syndrome in premature infants

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Abstract. Effects of early surfactant administration to premature newborns have been widely investigated in several RCTs. Furthermore, recent studies and metanalysis have compared early with delayed administration as well as selective and prophylactic use of surfactant. These data from the literature are discussed in the present review together with the factors that may argue against the standardization of respiratory care at birth. A tailored approach based on the stratification of risk factors may be appropriate in the so heterogeneous population of premature newborns. (www.actabiomedica.it)

Key words: premature newborns, early surfactant administration

What is known and controversial aspects

Early surfactant administration to preterm infants intubated for respiratory distress syndrome (RDS) is better than delaying administration to such infants until they develop worsening RDS. So states the last Cochrane metanalysis about the comparison between these two treatment modalities, the former of which leads to a decreased risk of acute pulmonary injury, chronic lung disease and neonatal mortality (1).

Nevertheless, the meaning of early surfactant administration needs further elucidation since it is a quite heterogeneous definition ranging from within the first 30 minutes of life to within 3 hours after delivery (2,3). Furthermore, this approach may be part of several different therapeutic strategies for RDS; of note, early administration may be selective, i.e. to infants with RDS, or prophylactic, that means to infants without RDS, but at risk of developing it (4-6).

Few years ago, tracheal intubation in the delivery room followed by mechanical ventilation (MV) and surfactant administration was a routine for the neonatologists providing care to extremely premature in-

fants. However, each of these procedures entails potential pitfalls and payoffs like hypoxemia, bradycardia, variations of intracranial pressure, airway injury, barotrauma and volutrauma (7,8). Early selective surfactant administration to infants with RDS followed by a short period of MV (less than 1 hour) and extubation to nasal continuous positive airway pressure (nCPAP) represents a modern and widely used strategy, known as INSURE method (intubation-surfactant-extubation), which allows to limit some of these factors (9, 10). This approach has been demonstrated to be better than selective surfactant replacement followed by continued MV with extubation from low ventilator support: it has been shown that infants with RDS managed with the INSURE approach are less likely to need MV, to develop BPD and to suffer from an air leak (11). Further evidence supporting early use of surfactant was provided by studies showing that even prophylactic administration reduced the risk of air leak and mortality compared to selective administration (12). However, more recent trials reflecting current practice (including greater use of maternal steroids and routine stabilization on nCPAP in the

delivery room) did not confirm these differences (4, 13). One of these studies, the CURPAP trial, compared early prophylactic INSURE approach (within 1 hour of life) to early nCPAP and rescue surfactant for nCPAP failures in spontaneously breathing infants between 25 and 28 weeks' gestation. No differences in mortality, incidence of air leak or CLD, need of MV during the first 5 days of life were observed between the two groups. Half of the infants in the nCPAP group were managed without intubation (4). Thus, selective surfactant administration after nCPAP failure may be an advisable approach for those infants who have received antenatal steroids and can be stabilized with nCPAP at birth. This means that a period of strict clinical observation is required to identify and treat infants with persistent or worsening RDS despite an early efficacious ventilation with nCPAP. At present, 2 hours after birth might be a reasonable time limit for infants born less than or equal to 29 weeks of gestation (6). In this way, it becomes feasible to establish whether a less invasive approach has created and is capable of maintaining a sufficient functional residual capacity or not.

Tailoring respiratory support at birth

We believe that further elucidations are needed before translating evidence from literature into daily practice. The variability of intra-uterine environment and fetal health, including the possible presence of chorioamnionitis, intra-uterine growth restriction, and incomplete antenatal steroid course, may argue against the standardization of early respiratory care. Furthermore, it is still unclear whether the suggestions from the aforementioned metanalysis are applicable to the lowest gestational ages since most RCTs excluded newborns younger than 25 weeks of gestation. Therefore, care of extremely immature lungs remains matter of investigation.

Despite gestational age may be used to stratify the level of respiratory care at birth, we believe that the "decision-making process" should also include a strict and repeated clinical assessment together with oxygen requirement trend monitoring during the first two "golden hours" of life.

At birth, as suggested by Jobe (14), the neonatologist can meet a newborn which may be considered a bad, marginal or good infant. This very interesting "start-classification", already promoted by other authors (15), implies a tailored approach at birth.

In our experience, bad infants should be intubated at birth because of the lack of respiratory drive. They are usually extremely preterm (<25 weeks) and/or characterized by a bad intrauterine environment. These patients usually require early surfactant administration before deciding whether they can be switched to nCPAP or mechanically ventilated after stabilization. Marginal infants show a sufficient respiratory drive able to be managed with a non-invasive support since birth. We think that they should include 25 week old newborn infants, although neonates with older gestational ages and bad intrauterine environment may be also considered. Marginal infants may become good infants if non-invasive ventilation responders or bad infants if they deteriorate within few hours from birth. In case of clinical deterioration and/or an oxygen requirement reaching 40% within two hours from birth, these babies should receive selective surfactant administration, therefore an "early surfactant", according to the INSURE method whenever possible. Good infants are those usually older than 25 weeks of gestational age without antenatal risk factors. They should be supported with nCPAP at birth since this approach is usually successful. Obviously, a minority of good infants may deteriorate needing more oxygen or increasing their respiratory effort. Rescue selective surfactant administration according to the INSURE method should be sufficient when nCPAP fails in these patients.

We believe this therapeutic approach based on stratification of risk factors and gestational ages should remain the optimal way to improve respiratory care at birth, as well as the whole intensive care of the so heterogeneous population of premature babies.

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