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Which clinical markers for appropriate timing of surfactant therapy?

Gianluca Lista, Francesca Castoldi
NICU - "V.Buzzi" Children's Hospital, ICP

Abstract. Preterm infants with RDS need adequate resuscitation maneuvers and appropriate timing of surfactant replacement but about the latter there is not an universal consensus. A correct evaluation should consider at the same time the administration of antenatal steroids, the radiological criteria, the clinical presentation, the FiO2 level, OI and a/ApO2. (www.actabiomedica.it)

Key words: surfactant, clinical markers, neonate

Introduction

Preterm infants need to be helped at birth to make foetal-neonatal transition with minimal risk for survival and quality of life. This is very important especially for extremely low for gestational age (ELGA) infants who are at high risk to develop respiratory distress syndrome (RDS) due to a reduced amount of surfactant and less efficacious spontaneous breathing. Therefore, physicians have to allow neonatal transition by performing adequate resuscitation maneuvers and choosing appropriate timing of surfactant replacement for preterm infants "at risk for RDS" or "with RDS".

In clinical practice, surfactant administration before the first breath seems not to reduce the incidence of bronchopulmonary dysplasia (BPD) and death, since the attempts to treat before the infants begin to breathe may interfere with the initial cardiorespiratory stabilization (1). Moreover at present many infants are not intubated in the delivery room (DR) and can be safely managed only with a non-invasive approach (e.g N-CPAP or N-IPPV) (2,3,4).

Therefore the prophylaxis with surfactant before the first breath or before the achievement of an early functional residual capacity (FRC) by the application of a CPAP (5) or other lung recruitment manoeuvres (e.g. Sustained Lung Inflation-SLI) is not indicated.

It is well recognized that surfactant reduces the critical transpulmonary pressure (P-tp= the difference between the alveolar pressure and the intrapleural pressure in the lungs) at which atelectasis occurs; moreover when natural surfactant is absent or diminished in amount, the P-tp is high and potentially dangerous. A high level of P-tp can interfere negatively on interstitial pressure inducing lung edema due to reduced lung fluid clearance and it may lead to a high risk of lung inflammation and air leak due to barovolutrauma (6). In course of mechanical ventilation (MV), the mean airway pressure (MAP) and tidal volumes are generally minimized for lung protection; there is evidence that this caution may not be enough to reduce lung injury due to stress and strain forces (7). Transpulmonary pressure represents true lung pressure, but it cannot routinely be measured in clinical practice, especially in preterm infants. The different modalities of respiratory support (both MV and non-invasive ventilation) are usually monitored with arterial blood gases and clinical signs of work of breathing (WOB) in according to gestational age and birth weight.

There is not an universal consensus about the right moment when surfactant should be given to re-

duce the risk of inappropriate P-tp both during non-invasive respiratory support with spontaneous breathing or MV. In this paper we shall try to identify clinical parameters to be used to research the optimal timing at least for the first dose of surfactant in preterm infants with RDS.

In course of spontaneous breathing the alveolar pressure (P-ao), corresponding to the atmosphere pressure (P-atm), is conventionally set at 0 cmH_2O. Under physiological conditions the P-tp is always positive, while the intrapleural pressure (P-ip) is always negative. In fact the P-ip measure is -8/-10 cmH_2O at the end-inspiration, while the P-tp measure at this time of the respiratory cycle is + 8/+10 cmH_20 [0-(-10/-8)]. On the other hand physiological P-tp is slightly positive (+ 5 H_2O) at end-exhalation, because the P-ip moves from -10 to -5 H_2O. The Silverman-Anderson score (assessment of presence and grade of chest and xiphoid retractions, expiratory gruntings and nasal flaring) is a useful tool for a clinical measure of the WOB of an infant with respiratory distress and it helps the physicians and nurses to evaluate the severity of respiratory distress and the pathological variations of the P-tp needed to obtain and maintain a normal lung volume and gas-exchange. Score 3 or less means minimal respiratory distress; score 4-5 means moderate distress; score 6 or more means severe respiratory distress.

While inhaling a room-air mixture (oxygen=20,9%; nitrogen=79% with an barometric pressure of 760 mmHg), the partial pressure of oxygen into the alveoli (PAO2) is 100 mmHg. An infant is considered well oxygenated if the Arterial blood oxygen tension (PaO2) level is maintained between 50 and 80 mmHg (50-80% of the oxygen moves from the alveoli to the arterial blood) with a normal value of CO2. If the same PaO2 levels are reached with a FiO2 of 0.30 the percentage of Oxygen moving from the alveoli to the systemic circulation is reduced to 30-50%; if the FiO2 is 0.4 the percentage drops to 25-30%.

In clinical practice, to evaluate the severity of the respiratory distress we use the arterial/alveolar oxygen tension ratio (a/APO2). The a/APO2 measures the PaO2/PAO2 and explains the amount of Oxygen transferred to the blood when compared to the oxygen available in the alveoli. A value < 0.75 is considered pathologic and <0.3 is found in a condition of severe respiratory failure (8).

In clinical practice, during MV, the MAP level can widely vary, but values >10 cmH20 can induce pneumothorax (9) by an excessive increase of the P-tp.

During respiratory support, the oxygenation index (OI) =(FiO2 x 100 x MAP)/(PaO2) is an important index to evaluate the severity of the respiratory distress and the clinical effect of the ventilator strategy. An OI =10 represents a low morbidity risk; OI >15, severe respiratory failure and high risk of mortality.

As we wrote above, a recent Cochrane metanalysis (5) concluded that a preterm infants at risk of RDS can be initially stabilized in DR with N-CPAP, but an early surfactant therapy has to be planned (especially in preterm infants with a gestational age below 24-25 wks' gestation just after first minutes of life or directly in DR).

In accordance with the above mentioned considerations and considering that a preterm infants during the first days of life can be maintained with SpO2 targets set at 88-92% (correlated to PaO2 of 45-70 mmHg) (10-11) we can try to define some practical guidelines to choose the more appropriate timing at least for the first dose of surfactant.

Indispensable and essential condition for the decision of administering surfactant, is the clinical presentation (tachi-dyspnea, cyanosis, expiratory grunting, etc) but also the contemporary presence of the typical radiological features of surfactant deficiency: small lung volume, air bronchogram and reticulo-granular infiltrations throughout the lungs. The radiological classification of RDS is graded in 4 stages, starting from the 1st one (slight reticulo-granular infiltrations), towards a progressive reduction of lung transparency and appearance of air bronchogram (2nd and 3rd stage) and arriving to the well known "white lung" (4th stage).

Therefore, once the radiological criteria have been satisfied, we should match them with the clinical presentation of respiratory failure (graded by the Silverman-Anderson score), the level of FiO2 to maintain the SpO2 targets (generally 88-92% in the acute phase of RDS for preterm infants with a GA<32 wks) and two indexes used to grade the severity of the res-

piratory distress (e.g. OI and a/ApO2, in order to consider oxygenation, level of carbon dioxide and mean airway pressure). Likewise, prenatal history and in particular antenatal steroids administration is of crucial importance, so it should be considered in this evaluation.

The physician needs a score to evaluate the need of first dose of surfactant replacement (as "early treatment", within the first 3 hours of life) in course of neonatal respiratory distress.

This score, in our opinion, should combine all the described variables and should be used routinely for surfactant need assessment. We are, at present, testing a score for this requirement.

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Correspondence:
Dr. Lista Gianluca
NICU- "V. Buzzi"
Children's Hospital, ICP