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Original article

Surfactant and mechanical ventilation

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Abstract. Even if non invasive respiratory support is widespread used in the management of respiratory failure, nevertheless mechanical ventilation and surfactant replacement are standard care for many preterm infants with respiratory distress syndrome (RDS). The interaction between exogenous surfactant and different modalities of ventilatory support are very important and can influence respiratory outcome. The optimization of surfactant replacement during respiratory support is crucial for the successful of this therapy. In course of mechanical ventilation lung recruitment manoeuvres before and after tracheal instillation of surfactant seem to facilitate its distribution and allow to obtain a more homogeneous lung volume. (www.actabiomedica.it)

Key words: surfactant, mechanical ventilation, lung recruitment manoeuvre, preterm

Artificial ventilation has proven to be a life-saving therapy for preterm infants with respiratory failure, but needs to follow some rules: ventilator parameters have to be set to reach the opening pressure of the immature lung, then they have to be adjusted to maintain an adequate ventilation through the choice of an appropriate tidal volume and PEEP to reduce the risk of lung injury (1).

Surfactant replacement therapy is standard of care for many preterm infants with RDS both in non-invasive ventilation (NIV) and mechanical ventilation (MV) since its introduction in the management of respiratory distress in 1990 (2,3). Both the administration of exogenous surfactant and the use of different modalities of ventilatory support can influence short- and long-term outcomes of preterm infants with respiratory distress (4).

Surfactant reduces the surface tension of the alveolus and the pressure needed to open the alveoli and to maintain them open with the achievement of an early FRC and the consequent improvement of compliance and lung volume.

The numerous clinical trials performed until now have not completely answered some very important questions about surfactant administration. The appropriate timing, the indication to administer it as a prophylaxis or as a therapy, the optimization of its efficacy with different ventilatory strategies remain controversial. After its tracheal instillation, exogenous surfactant is processed by the alveoli and the function of this treatment is improved by metabolic processing. The preterm animal seems to be penalized, because the surfactant is intrinsically abnormal when compared to that of the adult (5). The clinical response to surfactant replacement depends from the biophysical characteristics of surfactant but also from its distribution into the lung. The optimization of surfactant replacement obtained by an adequate respiratory support is crucial for the efficacy of this therapy.

The atelectatic lung showed to contain less surfactant, after a replacement treatment, than the partially or full aerated one: therefore it seems that the lung needs to be recruited before the administration of surfactant, so that the surfactant itself can be pushed through the airways till the alveoli (6). The "first lung recruitment manoeuvre" has to be performed just after birth to obtain a more homogenous lung volume and to reduce the risk of lung injury. Sustained lung infla-

tion (SLI), when applied at birth to win the high airway resistance and therefore the long time constant of the liquid filled lung, facilitates transition from foetal to neonatal life in an animal model (7). The removal of the fluid from the lung immediately after birth allows the achievement of an early functional residual capacity (FRC). The optimal technique of lung recruitment at birth still remains under investigation. Recent unpublished animal data showed that a stepwise PEEP incremental manoeuver at birth titrated to patients' lung mechanics was practical and showed short-term results similar to a surfactant-repleted lung (8). This first lung recruitment manoeuvre (LRM) may be considered the pre-requisite to allow the surfactant to reach a large amount of alveoli, to begin its action and to promote a more uniform lung volume. This LRM is the first step of an high lung volume strategy that is the key to protect the neonatal lung during mechanical ventilation (9). For this reason, when assisting very preterm infants at risk for RDS in the delivery room, it may be useful to do a first lung recruitment manoeuvre with SLI with fixed or growing PEEP levels, in order to clear the lung from the fluid and to achieve an early FRC, before giving surfactant. On the contrary a ventilation without an high lung volume strategy from the first breath may lead to a partial clearing of lung fluid and to a non-homogenous air-filling that can have a negative influence on surfactant distribution (10). Further clinical trials are needed to investigate these suggestions.

Surfactant delivered to the lung has to be evenly distributed and besides a quick administration in an adequate volume, a practical way to improve surfactant distribution is to maintain an optimal ventilatory strategy.

In animals it has been demonstrated that a recruitment manoeuvre performed after surfactant administration improves all lung function indices, but when surfactant is given without prior volume recruitment, only the a/ApO_2 ratio shows an improvement. These results support the hypothesis that a volume recruitment strategy enhances the effectiveness of surfactant replacement by facilitating its distribution (11).

In an other animal study, it has been demonstrated that, when the optimal end-expiratory pressure to open the lung is established, the spatial distribution of ventilation in the lavaged lung is significantly modified by a recruitment manoeuvre performed after surfactant administration. No further recruitment was obtained maintaining the end-expiratory pressure at the same level as before surfactant (12).

Therefore a "*second lung recruitment manoeuvre*" seems to be necessary to optimize surfactant distribution and lung volume in all preterm infants in mechanical ventilation (both in HFOV or CMV) for RDS.

The choice of the optimal lung volume strategy has become routine practice during HFOV: the application of a lung recruitment manoeuvre (LRM) obtained by the progressive increase of mean airway pressure (MAP) or continuos distending pressure (CDP) is widely accepted to guarantee the efficacy of this ventilation (13,14) and in particular the administration of two LRM before and after surfactant replacement has been applied with success in preterm infants in HFOV for RDS (15). In experimental study the research of the optimal PEEP in course of targeted volume ventilation led to the optimization of the lung volume (16). This strategy has been applied in clinical practice reproducing the same concept of "double" LRM (before and after surfactant) used in course of HFOV. In a pilot study conducted in preterm infants in volume guarantee ventilation for acute RDS, the use of a double LRM strategy (SLI in the delivery room plus LRM with PEEP incremental/decremental trial to search the optimal PEEP) led to the earlier lowest FiO_2 of the first 12 hours of life and to a shorter O_2 dependency (17). The Authors speculated that LRM applied to preterm lung with RDS enhances the effectiveness of surfactant replacement therapy by facilitating the distribution of instilled surfactant. Further large clinical trials are needed to confirm this hypothesis.

In conclusion, surfactant replacement is crucial in the management of respiratory distress of preterm infants, and a high lung volume strategy during mechanical ventilation (before and after surfactant administration), seems to play a critical role in enhancing the effect of surfactant on lung mechanics and lung volume distribution.

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