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Surfactant and non invasive ventilation for preterm infants

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Abstract. Mechanical ventilation, although life-saving, predisposes preterm infants to BPD. NCPAP emerged as an alternative to invasive ventilation, but it fails in about 30% of infants even when coupled with surfactant therapy. Alternative modes of non invasive ventilation are currently used in neonatology in order to prevent mechanical ventilation. Among these, Synchronized Nasal Intermittent Positive Ventilation (SNIPPV) seems to ensure better results. (www.actabiomedica.it)

Key words: surfactant, CPAP, non invasive ventilation, preterm infant

Introduction

Endotracheal intubation and mechanical ventilation (MV), or "invasive ventilation", have been the prevailing intervention for neonates with respiratory distress syndrome (RDS) over the last 40 years. This approach, although life-saving, is a major factor predisposing to bronchopulmonary dysplasia (BPD). The introduction of surfactant therapy in early '90s significantly reduced mortality infants with RDS (1) but, although effective in the acute phase of the disease, this could not reduce the overall incidence of BPD. In the last decade NCPAP, that has been demonstrated as safe as routine intubation for preterm infants (2-4), emerged as an alternative to invasive ventilation. Although the widespread use of NCPAP redefined the respiratory care of preterm infants, approximately 50–67% of NCPAP treated infants develop a respiratory failure that requires an higher ventilatory support (5). For some of these infants MV can be avoided by coupling NCPAP with exogenous surfactant administered by the INSURE (Intubation SURfactant Extubation) technique. Nevertheless, approximately 25-38% of VLBW infants fail NCPAP combined with surfactant therapy, resulting in re-intubation and MV (5). Alternative modes of non invasive ventilation (NIV) are now used in neonatology in order to provide a greater level of respiratory support than does NCPAP and further prevent invasive ventilation in a larger fraction of infants.

Delivery room respiratory support

Delivery room (DR) NCPAP and surfactant use were investigated in 3 randomized controlled trials (RCTs): the COIN trial (2), the SUPPORT trial (3) and the VON trial (4). Overall, these trials suggested that NCPAP as first line respiratory support results in no differences in relevant short term outcomes when compared with intubation and MV, but it may prevent or shorten the duration of respiratory support. Contrary to expectations, although the rate of intubation for NCPAP treated infants was 46%, 83,1% and 52% respectively, none of these trials could demonstrate a reduction in BPD rate using non invasive respiratory

support. Recently, the CURPAP trial aimed to evaluate the efficacy of combining prophylactic surfactant and early NCPAP in very preterm infants (6). 208 infants born at 25-28 weeks managed with NCPAP from birth were randomized in the DR to either prophylactic surfactant followed by immediate extubation or to NCPAP followed by rescue surfactant if oxygen requirements were >40%. The need for MV in the first 5 days of life was similar in both groups (31.4% vs. 33.0%) as well as mortality, BPD and the incidence of air leaks.

The "sustained lung inflation" maneuver has been recently introduced as part of the respiratory management for preterm infants at birth, with the aim of improving FRC development by allowing an appropriate time-constant for the air/liquid interface to move into the distal airways. This approach performed at birth and followed by NCPAP has been demonstrated to reduce the need for intubation and surfactant and the BPD rate when compared with NCPAP alone (7).

Surfactant and NCPAP

Despite the proven benefits, NCPAP not always offers sufficient ventilatory support to attain adequate ventilation. In some infants, MV can be avoided by coupling NCPAP with exogenous surfactant given by INSURE technique. According to this procedure, surfactant is administered by an intubation followed by a rapid extubation. Although this technique is largely used and proven to reduce MV need (1), the optimal timing and delivery mode of surfactant remain uncertain. In ventilated preterm infants early surfactant treatment (≤ 2 hrs of life) reduces the risk of air leaks, mortality and BPD when compared with delayed therapy (8). For infants on NCPAP, surfactant administration is often guided by the FiO_2 level needed to maintain a suitable SpO_2. Also in this case surfactant is more effective if given as early rescue, at FiO_2 0.3-0.35, than as a delayed treatment (1). In infants of 27-31 weeks' gestation, NCPAP at birth combined with surfactant given within the first hour of life reduces the need for MV and the incidence of air leaks and BPD versus NCPAP alone (9), confirming that an early rescue strategy is important. Furthermore, as there are no clinically adequate predictors of early NCPAP failure at time of admission to the NICU, a test for lung maturity predicting the development of severe RDS would be a suitable tool to guide correct and early surfactant administration. Lamellar body count in gastric aspirate has recently been reported to be very promising. Moderate-to-severe RDS can be predicted by this test with a sensitivity and specificity of 73-92% (1).

To date, an intubation is generally needed for surfactant administration. Endotracheal intubation is a traumatic and painful procedure that usually requires sedation and can be associated with many adverse effects. A proposed alternative - is to give surfactant by inserting a thin catheter into the trachea. This minimally invasive technique, generally performed by direct laryngoscopy without analgesia, has been proven to be a valid alternative to the "classic" INSURE strategy in a recent RCT(10).

Surfactant and NIV

As approximately 25-38% of infants treated with NCPAP coupled with surfactant fail this strategy, alternative modes of NIV are currently used in neonatology in order to prevent MV in a larger fraction of neonates.

Bilevel Positive airway pressure (BiPAP) is a form of non invasive ventilatory support that assists spontaneous breathing alternating an high and low level of CPAP at preset intervals. In a retrospective study, BiPAP reduces MV need in infants who fail NCPAP following INSURE therapy (11) and it decreases the length of respiratory assistance, O_2 therapy and hospital stay when used as primary form of respiratory support (12).

NIPPV is a non invasive mode of ventilation that offers superimposed breaths on NCPAP. Breaths may be synchronized (SNIPPV) or not to the infant's respiratory efforts. Although a recent retrospective study suggests no differential impact on clinical outcomes between NIPPV and SNIPPV (13), several observations favour SNIPPV. During NIPPV tidal volume increases only when pressure peaks occur during spon-

taneous inspiration, indicating that synchronisation is beneficial (14). Delivering the pressure peak immediately after the start of a spontaneous inspiration, when the glottis is open, makes the pressure being effectively transmitted to the lungs rather than to the oesophagus, obtaining the double advantage of increasing tidal volumes and reducing the risk of gastrointestinal distension.

Moreover, thoraco-abdominal asynchrony and WOB are significantly decreased during SNIPPV when compared with NIPPV and NCPAP (5, 15, 16). Synchronized and non-synchronized NIPPV has been tested in several trials to treat RDS (5, 17), also in association with surfactant therapy. Results suggest clinical benefit from this mode of ventilation, compared with NCPAP, in terms of MV need, duration of MV and rate of BPD.

In clinical practice we use flow-synchronized NIPPV obtained by means of a flow-trigger system, developed by our group, which maintains stable the flow signal despite the leaks from patient's mouth. This device has been successfully used in VLBW infants after extubation (18). We tested flow-SNIPPV coupled with the INSURE technique as primary mode for RDS in 33 preterm infants of <32 weeks' gestation and compared the results with a series of 31 infants of the same GA treated with the NCPAP/INSURE strategy. The SNIPPV/INSURE approach was able to reduce MV need from 35.4% to 6.1% (p=0.038, personal data).

Conclusions

NIV strategies may provide a greater level of respiratory support than NCPAP, thus preventing intubation and MV in a larger number of infants. Among these, SNIPPV seems to ensure better results. Even if it is unlikely that NIV will completely obviate invasive ventilation, it may reduce the need for repeated intubation and prolonged ventilation and their related complications that mostly affect the sensitive population of VLBW infants.

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