Open lung high frequency ventilation in preterm infants with respiratory distress syndrome: practical considerations and recommendations

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Chapter 8

Summary, conclusion and future perspectives
Summary

Chapter 1 provides an outline of the consequences of mechanical ventilation in the preterm infant with respiratory distress syndrome (RDS) and the options to improve ventilation strategies, and thus pulmonary morbidity. Improved survival of the preterm infant was only possible with the introduction of mechanical respiratory support. The other side of this success was the apparition of bronchopulmonary dysplasia (BPD), a chronic pulmonary disease typical of the premature infant with important health consequences including the increased risk of neurodevelopmental impairment. The causality between BPD and ventilator induced lung injury resulted in the quest for the improvement of ventilatory strategies through the patho-physiological understanding of lung injury and BPD. The concept of open lung ventilation (OLV) in which both, overinflation and atelectasis are avoided, was developed. Unfortunately the application of OLV in clinical studies did not result in a decrease of the incidence of BPD. Analysis of the human studies raises questions on the appropriate application of the OLV strategy. In animal studies the protective effect of OLV has been clearly demonstrated compared to the human clinical trials. The question is whether it is possible to further refine and thoroughly apply the OLV strategy using high frequency ventilation (HFV), to the right patient at the right time during daily clinical practice.

In preterm infants Early Nasal Continuous Positive Airway Pressure (ENCPAP) reduces the need for invasive mechanical ventilation and surfactant therapy, but not the combined outcome death or BPD. Almost half of the infants fail ENCPAP in the first days and the first surfactant dose is given as a late rescue treatment (> 6 hours after birth) which is known to increase the risk of death and/or BPD compared to early rescue surfactant. Early prediction of patients who will fail ENCPAP is important to prevent late surfactant rescue therapy as this is less effective than the early rescue treatment to reduce mortality. Chapter 2 shows that combining gender, birth weight and the fraction of inspired oxygen at 1 and 2 hours of age allows for a better and more individualized prediction of ENCPAP failure in preterm infants less than 30 weeks gestation. This model needs to be validated in a prospective cohort study.

Chapter 3 explores the effect of OLV using both positive pressure ventilation and high frequency oscillatory ventilation on gas exchange and ventilator induced lung injury in newborn piglets. The surfactant lavage RDS model was used in piglets which were ventilated for 5 hours with both ventilation techniques. The control group consisted of conventionally ventilated piglets. Compared to conventional ventilation OLV ventilation groups had a significantly better gas exchange, less ventilator induced lung injury and better lung mechanics. There was no difference between both OLV groups, emphasizing
that not the ventilator but the ventilation strategy counts.

Chapter 4 describes that changes in oxygenation can be used to guide the recruitment procedure during open lung HFV and that optimal recruitment allows ventilation with little or no supplemental oxygen (FiO2 ≤ 0.25) in the majority of preterm infants with neonatal RDS. The present study seems also to indicate that hysteresis is present in the early phase of neonatal RDS. The continuous distending pressure could be lowered significantly before oxygenation started to deteriorate, indicating loss of lung volume due to alveolar/saccular collapse. Furthermore detailed information on the pressures needed to recruit and stabilize the lung before and after surfactant treatment in neonatal RDS are described for the first time.

In chapter 5 the performance of the individualized, oxygenation guided OLV procedure is described in detail. The study provides valuable and practical information for clinicians aiming to implement open lung HFV in their daily clinical practice. It shows that such a ventilation strategy is time consuming but it also shows that it can be shortened by transferring the responsibility of ventilation management to a selective group of trained professionals. The latter may be of interest for units working with physician assistants or respiratory therapists.

Radiological characteristics of RDS are dependent on the respiratory therapy that is applied. In chapter 6 it is demonstrated that an individual oxygenation guided recruitment procedure during HFV in preterm infants with RDS improves radiological radiolucency and this further improves significantly after surfactant treatment. Radiological signs of hyperinflation are rare and, when present, often mild and not resulting in air leaks. These data indicate that the classical RDS scoring systems cannot be used to assess severity of lung disease in preterm infants with RDS when the OLV ventilation strategy is used. More importantly, also from a radiological perspective open lung HFV is safe in preterm infants with RDS.

Specific data on how to apply HFV in daily clinical practice are still limited and mainly consist of general recommendations such as to optimize lung volume and to avoid crossover to conventional mechanical ventilation by weaning patients from HFV until extubation. Detailed data on the extubation process during HFV in preterm infants are lacking. Chapter 7 describes the feasibility of extubation in the majority of infants weaned from open lung HFV with criteria to attempt the extubation set at a continuous distending pressure ≤ 8 cm H2O and a FiO2 ≤ 0.3 with a success rate > 90%.
Conclusions

In premature infants ventilated because of RDS the favorable effect of HFV OLV compared to conventional mechanical ventilation on the incidence of BPD remains a matter of debate. An important lack in published human studies is the clinical practice surrounding the thorough application of OLV with HFV from the acute stage of RDS through the weaning process until extubation.

Studies in this thesis demonstrate that applying a “full package” OLV from start to finish in respiratory failure with high frequency ventilation is feasible and safe in preterm infants with RDS. Lung hysteresis is present which stresses the importance to decrease the pressure after the recruitment maneuver. As surfactant therapy changes lung characteristics pressures should be adjusted timely after surfactant instillation to prevent overinflation. The need for these individualized adjustments is more time consuming but, when applied by trained medical staff the personnel resources can be reduced. Also the radiological evaluation of the chest is different especially with regard to the gradation of the severity of RDS. Classical radiological characteristics of RDS can not be used as radiolucency is improved. Mild hyperinflation is found in only a minority of patients on chest X-ray. Finally, cross over from OLV HFV to conventional mechanical ventilation can be avoided as it is possible to wean and to extubate patients directly from HFV.

Future perspectives

To ascertain if the application of the OLV strategy further improves the survival of the very preterm infants without BPD, a randomized controlled trial with a correctly applied and documented OLV strategy has to be performed. There is no “one fits all” adjustment of the ventilation settings to recruit and to maintain recruited the lung without overdistention. The OLV procedure as described in this thesis is the first step that should be properly taught and trained to the medical staff members performing the OLV strategy, before a clinical trial can be started.

A randomized trial would ideally include infants at high risk of death and/or BPD with respiratory failure and who need mechanical ventilation. The intervention group is assigned to the immediate and uninterrupted application of OLV strategy with HFV. The control group is assigned to the current “gentle” conventional ventilation strategies with sufficient PEEP and low tidal volumes but without recruitment maneuver. HFV should be used as it is relatively simple to use, both for the recruitment - derecruitment process and for the delivery of small tidal volumes. The standardized but individualized OLV procedure should be strictly protocolized as well as the weaning and extubation criteria for all mechanical ventilation episodes during neonatal admission. The ventilation protocol should enclose well defined endpoints to evaluate the ventilation and
oxygenation strategy for both treatment arms. Data on relevant ventilation parameters should be reported in order to assess if the intervention was properly applied. The ventilation mode used would remain the mode of the initial treatment arm and crossover of ventilation strategy should only be allowed under very strict conditions of potential lethal respiratory failure.

One of the real difficulties in the daily use of OLV HFV is due to the lack of a reliable, easy to use and bedside lung volume measurement tool. Today second bests are used and multiple data need to be integrated at all (some stressful) times to perform the OLV procedure. New technologies as respiratory inductive plethysmography and electrical impedance tomography are promising diagnostic tools for the future. Combining and integrating data from these technologies with ventilator settings, pulsoximetry and transcutaneous carbon dioxide data could further improve and facilitate the whole procedure of recruitment – derecruitment – optimizing pressures and thereby help the respiratory therapist in this complex procedure.

The developmental immaturity and vulnerability of premature infants represent major challenges to further reduce pulmonary morbidity. Studies of this thesis demonstrate that the continuous application of the OLV strategy during daily care is feasible and safe but needs a change in mindset with regard to “setting the ventilator”. Future research on the reduction of BPD should incorporate the thorough application of the open lung ventilation strategy if mechanical ventilation is indicated.