www.jpeds.com • THE JOURNAL OF PEDIATRICS

Relationship between Mean Airways Pressure, Lung Mechanics, and Right Ventricular Output during High-Frequency Oscillatory Ventilation in Infants

Emanuela Zannin, PhD[1], Daniela Doni, MD[2], Maria Luisa Ventura, MD[2], Tiziana Fedeli, MD[2], Camilla Rigotti, PhD[2], Raffaele L. Dellacá, PhD[1], and Paolo E. Tagliabue, MD[2]

Objective To characterize changes in lung mechanics and right ventricular output (RVO) during incremental/decremental continuous distending pressure (CDP) maneuvers in newborn infants receiving high-frequency oscillatory ventilation, with the aim of evaluating when open lung maneuvers are needed and whether they are beneficial.

Study design Thirteen infants on high-frequency oscillatory ventilation were studied with a median (IQR) gestational age of 26^1 (25^3-29^1) weeks and median (IQR) body weight of 810 (600-1020) g. CDP was increased stepwise from 8 cmH_2O to a maximum pressure and subsequently decreased until oxygenation deteriorated or a CDP of 8 cmH_2O was reached. The lowest CDP that maintained good oxygenation was considered the clinically optimal CDP. At each CDP, the following variables were evaluated: oxygenation, respiratory system reactance (Xrs), and RVO by Doppler echocardiography.

Results At maximal CDP reached during the trial, 19 [1] cmH_2O (mean [SEM]), oxygenation markedly improved, and Xrs and RVO decreased. During deflation, oxygenation remained stable over a wide range of CDP settings, Xrs returned to the baseline values, and RVO increased but the baseline values were not readily restored in all patients.

Conclusion These results suggest that Xrs and RVO are more sensitive than oxygenation to overdistension and they may be useful in clinical practice to guide open lung maneuvers. *(J Pediatr 2017;180:110-5).*

High-frequency oscillatory ventilation (HFOV) is a respiratory support strategy that has been applied widely in newborns with respiratory failure. HFOV optimally applied aims to recruit the lung to total lung capacity (TLC) and then to apply ventilation on the deflation limb of the pressure–volume curve (open lung strategy).[1-7] To achieve TLC, however, transient but relatively high values of continuous distending pressure (CDP) are required, which may be associated with deterioration of pulmonary blood flow[8-11] and lung tissue distension.[3,4,12,13]

Although there is consensus on the use of an open lung approach on commencement of HFOV, in clinical practice there are still difficulties in evaluating whether subsequent open lung maneuvers are needed. These difficulties arise from concerns about the effect of distending pressure on cardiopulmonary function and from concern for lung overdistention.

At the bedside, open lung maneuvers normally are guided by changes in peripheral oxygen saturation (SpO_2); however, it has been shown that changes in SpO_2 are very subtle throughout a wide range of pressure settings,[14-16] which limits its usefulness in determining whether unnecessarily high levels of pressure are applied.

The availability of noninvasive tools that allow direct assessment of pulmonary blood flow and lung mechanics during HFOV at the bedside are of crucial importance to make open lung maneuvers safer and tailored to the characteristics of individual patients. Doppler ultrasonography scanning is a noninvasive tool that currently is used in clinical practice for the evaluation of the cardiopulmonary function in preterm infants. Specifically, right ventricular output (RVO) assessed by Doppler ultrasonography scanning was found to be the hemodynamic variable most sensitive to

CDP	Continuous distending pressure
CDPmax	Maximal CDP reached during the trial
CDPopt	Optimal CDP
E_{X5}	Elastance derived from reactance evaluated at 5 Hz
E_{Xfosc}	Elastance derived from reactance evaluated at the prevailing oscillatory frequency
FiO_2	Fraction of inspired oxygen
fosc	Oscillatory frequency
FOT	Forced oscillation technique
HFOV	High-frequency oscillatory ventilation
RVO	Right ventricular output
SpO_2	Peripheral oxygen saturation
TLC	Total lung capacity
Xrs	Respiratory system reactance
X5	Xrs evaluated at 5 Hz

From the [1]Department of Electronics, Informatics and Bioengineering, Politecnico di Milano University, Milan, Italy; and [2]Neonatal Intensive Care Unit, Fondazione MBBM, Monza, Italy

Politecnico di Milano University (E.Z. and R.D.) has a pending patent on the use of FOT for the detection of lung volume recruitment. The other authors declare no conflicts of interest.

http://dx.doi.org10.1016/j.jpeds.2016.09.015

changes in CDP in infants receiving HFOV during initial lung recruitment.[10]

A promising tool for the noninvasive assessment of lung mechanics in mechanically ventilated subjects is the forced oscillation technique (FOT). FOT measures the mechanical impedance of the respiratory system by evaluating its response to pressure oscillations. Respiratory system impedance commonly is expressed in terms of resistance and reactance (Xrs), which in turn represents the elastance (1/compliance) and inertia of the system. FOT has been used successfully to evaluate changes in lung mechanics during inflation/deflation maneuvers.[17] In particular, it has been shown that changes in Xrs, associated with changes in the distending pressure of the lung, indicate lung volume recruitment and lung tissue distension.[3,13,18] Moreover, during HFOV, Xrs measurements can be obtained without suspending ventilation or modifying the CDP.[4,7]

The aims of the present study were to characterize changes in Xrs and RVO during incremental/decremental CDP maneuvers in newborn infants receiving HFOV and to evaluate whether the use of these variables, in conjunction with SpO_2, may help in guiding CDP maneuvers.

Methods

All measurements were performed in the neonatal intensive care unit of Fondazione MBBM-Ospedale San Gerardo, Monza, Italy. The study was approved by the local ethics committee, and informed parental consent was obtained before the studies.

All infants receiving HFOV for respiratory failure, excluding those with major congenital malformations, were eligible. Infants were tested if they were considered hemodynamically stable by the attending physician (estimated pulmonary arterial pressure < 20-30 mm Hg). Infants were sedated but not paralyzed. Infants were treated with inotropic support and/or inhaled nitric oxide if required. No supplemental fluids were provided either before or during the distending maneuver.

Ventilatory Strategy

HFOV was generated by a SensorMedics 3100A (Carefusion, Yorba Linda, California). Pressure amplitude and oscillatory frequency (fosc) were kept at the clinically set values. An open lung maneuver was conducted specifically for the study as follows: starting at a CDP of 8 cmH_2O, CDP was increased every 5 minutes by 2 cmH_2O. The fraction of inspired oxygen (FiO_2) was reduced stepwise, keeping SpO_2 within the target range (88%-94%). The incremental CDP series was interrupted when SpO_2 no longer improved or the FiO_2 was ≤0.25 (maximal CDP reached during the trial, or CDPmax). CDP was then decreased until oxygenation deteriorated or CDP reached 8 cmH_2O.[19] At the end of each CDP step, fosc was reduced to 5 Hz for 10 seconds for the assessment of Xrs at 5 Hz.

When fosc was reduced to 5 Hz, pressure amplitude was adjusted to limit tidal volume. At the end of the CDP trial, the clinically optimal CDP (CDPopt) was identified as the lowest CDP that was able to maintain adequate oxygenation. If CDP could be reduced to 8 cmH_2O without compromising oxygenation, 8 cmH_2O was designated as CDPopt.

Measurements and Monitoring

SpO_2, transcutaneous partial pressure of oxygen, transcutaneous partial pressure of carbon dioxide, heart rate, and arterial blood pressure were monitored throughout the recruitment procedure. In infants with patent ductus arteriosus both pre- and postductal SpO_2 were monitored to evaluate possible right-to-left shunting, and preductal measurements were considered for data analysis. At the end of each CDP step, the following measurements were performed: lung mechanics by FOT and RVO by echocardiography. The equipment for FOT consisted of pressure and flow sensors placed at the proximal end of the endotracheal tube.[4]

Doppler echocardiography was performed by an ultrasound imaging system with a 4-12 MHz vector array transducer (Philips iU33; Philips Healthcare, Eindhoven, The Netherlands). All measurements were performed by one observer (D.D.), as described in literature.[20]

Data and Statistical Analyses

The Sp_{O2}/FiO_2 ratio was calculated to evaluate oxygenation at different protocol steps. Xrs was estimated from the pressure and flow signals by use of the cross-spectrum method.[21] Xrs was evaluated both at the prevailing fosc and at 5 Hz (X5, ie, Xrs evaluated at 5 Hz) and used to estimate respiratory system elastance. Tidal volumes were computed by integrating the flow signal.

RVO was calculated with the following formula[20] and normalized for the body weight:

$$RVO = \frac{VTI \times \pi \times D^2 \times HR}{4}$$

where VTI is the time integral of the blood flow velocity in the pulmonary artery and D is the diameter of the pulmonary artery.

All data were tested for normality. Significance of differences at different CDP steps was evaluated by 1-way ANOVA for repeated measurements or by the equivalent nonparametric test as appropriate. Holm-Šídák or Tukey post hoc tests were used as appropriate. *P* values smaller than .05 were considered statistically significant.

Results

Thirteen preterm infants (9 male and 4 female) with a median (IQR) gestational age of 26^1 (25^3-29^1) weeks, postnatal age of 2 (1-3) days, and body weight of 810 (600-1020) g were studied. At the time of the study infants had been on HFOV for a median (IQR) of 31 (15-54) hours. In all infants, HFOV was used as a first intention mode as per unit policy. At baseline, infants were ventilated with a median (IQR) CDP of 12 (12-13) cmH_2O, a FiO_2 of 0.40 (0.28-0.60), fosc of 15 (12-15) Hz, and a pressure amplitude of 33 (28-39) cmH_2O. At the time of the study, 5 infants were receiving continuous