Regional Volume Characteristics of the Preterm Infant Receiving First Intention Continuous Positive Airway Pressure

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Objective To determine whether applying nasal continuous positive airway pressure (CPAP) using systematic changes in continuous distending pressure (CDP) results in a quasi-static pressure–volume relationship in very preterm infants receiving first intention CPAP in the first 12-18 hours of life.

Study design Twenty infants at <32 weeks' gestation with mild respiratory distress syndrome (RDS) managed exclusively with nasal CPAP had CDP increased from 5 to 8 to 10 cmH_2O, and then decreased to 8 cmH_2O and returned to baseline CDP. Each CDP was maintained for 20 min. At each CDP, relative impedance change in end-expiratory thoracic volume ($\Delta ZEEV$) and tidal volume (ΔZV_T) were measured using electrical impedance tomography. Esophageal pressure (P_{oes}) was measured as a proxy for intrapleural pressure to determine transpulmonary pressure (P_{tp}).

Results Overall, there was a relationship between P_{tp} and global $\Delta ZEEV$ representing the pressure–volume relationship in the lungs. There were regional variations in $\Delta ZEEV$, with 13 infants exhibiting hysteresis with the greatest gains in EEV and tidal volume in the dependent lung with no hemodynamic compromise. Seven infants did not demonstrate hysteresis during decremental CDP changes.

Conclusion It was possible to define a pressure–volume relationship of the lung and demonstrate reversal of atelectasis by systematically manipulating CDP in most very preterm infants with mild RDS. This suggests that CDP manipulation can be used to optimize the volume state of the preterm lung. *(J Pediatr 2017;187:80-8).*

Continuous positive airway pressure (CPAP) is now recommended as the initial respiratory support for spontaneously breathing preterm infants.[1,2] However, practical recommendations for setting the continuous distending pressure (CDP) are lacking. Practices vary widely with reported CPAP levels between 3 and 10 cmH_2O.[3-5] Higher pressures may contribute to adverse events such as pneumothorax, but inadequate pressures may result in atelectasis and chest wall distortion.[4,6] Avoiding atelectasis and overdistension are important for the prevention of lung injury.[7,8] Fundamentally, the optimal initial CDP should be set to each infant's needs and will be dependent on degree of atelectasis, chest wall compliance, and respiratory drive. Equally important is adjusting CDP as lung disease evolves. Although there is agreement on the indications for CPAP, there is little evidence to guide clinicians in determining the optimum CPAP level.

CPAP improves gas exchange by increasing end-expiratory lung volume (EELV) and improving breathing patterns.[9-11] The effect of CDP on EELV in preterm infants has been widely studied,[9,10,12-14] but the mechanism of change in EELV remains unclear, with some studies showing increased EELV with increased CDP and others not doing so.[9,10,15] This may be because previous studies have failed to consider the interaction between CDP and the volume state of the lung, which is particularly pertinent to the surfactant-deficient, poorly compliant, atelectatic preterm lung with respiratory distress syndrome (RDS). In the atelectatic lung, effective ventilation and work of breathing rely on a sufficient positive end-expiratory pressure (PEEP).[16,17]

Optimal ventilation requires using a dynamic PEEP approach with an open lung strategy that exploits hysteresis and applies ventilation on the deflation limb of the quasi-static pressure–volume (P-V) relationship of the lung.[18-20] In infants with severe RDS ventilated using high-frequency oscillatory ventilation (HFOV), open lung strategies that use stepwise changes in distending pressure have been shown to

ARDS	Acute respiratory distress syndrome	PEEP	Positive end-expiratory pressure
AU	Arbitrary units	P_{oes}	Esophageal pressure
CDP	Continuous distending pressure	P_{tp}	Transpulmonary pressure
C_{dyn}	Dynamic compliance	P-V	Pressure–volume
CPAP	Continuous positive airway pressure	RDS	Respiratory distress syndrome
EELV	End-expiratory lung volume	RR	Respiratory rate
EIT	Electrical impedance tomography	SpO_2	Oxygen saturation
fEIT	Functional electrical impedance tomography	Tc_{CO2}	Transcutaneous carbon dioxide
		V_T	Tidal volume
FiO_2	Fraction of inspired oxygen	$\Delta ZEEV$	Impedance change in end-expiratory thoracic volume
HFOV	High-frequency oscillatory ventilation		
HR	Heart rate	ΔZV_T	Impedance change in tidal volume
P_{aw}	Mean airway pressure		

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open collapsed lung regions and to improve the homogeneity of ventilation, EELV, and compliance, thus improving gas exchange.[18,20] In children, PEEP recruitment strategies using conventional ventilation have shown reversal of atelectasis in dependent lung areas,[21] but data are lacking regarding the use of PEEP manipulation using conventional ventilation in the neonatal population. In animal studies, these approaches have been shown to reduce lung injury.[22,23] An important finding of those studies was that no single PEEP level will optimize respiratory support. Furthermore, a response to lung recruitment maneuvers is not seen in all patients with atelectatic lung disease.[21] This may be more important in preterm infants receiving CPAP, whose lung disease is less severe than that of infants needing intubation, and where a leak around the CPAP nasal interface may compromise reliable CDP delivery. The relationship between CDP and lung volume may have clinical implications in the management of these infants. Thus, we sought to determine whether hysteresis could be demonstrated by manipulating CDP using CPAP in early preterm lung disease.

Methods

This study was performed at The Royal Women's Hospital, Melbourne, Australia and was approved by the institution's Research Ethics Committee. Informed written parental consent was obtained prospectively for each infant. Infants were studied supine, in quiet sleep if they were <32 weeks' gestation, 12-18 hours of age, and were receiving first intention nasal CPAP (BabyLog 8000 Plus; Dräger Medical, Lübeck, Germany) for RDS, and requiring a fraction of inspired oxygen (FiO_2) <0.4 to maintain a preductal oxygen saturation (SpO_2) of 88%-92%. Infants were not studied if they had a congenital anomaly, were receiving nasal intermittent positive pressure ventilation, had a confirmed air leak, or had skin too fragile for electrocardiography electrode placement.

CPAP settings before study commencement were determined by the clinical team. The Dräger BabyLog 8000 Plus mechanical ventilator operating in CPAP mode with the flow set at 8L/min, connected to a CPAP circuit and humidifier (RT circuit and MR850 humidifier; Fisher and Paykel Healthcare, Auckland, New Zealand) was used to provide CPAP. The short Hudson CPAP binasal prong system (Teleflex Medical, Research Triangle Park, North Carolina) was used as the nasal interface and secured with a hat (CPAP CAP System; Austranter Medical System, Canberra, Australia). Chin straps were not used to aid mouth closure.

Infant demographic and clinical data, including gestation, birth weight, sex, age at study, CPAP levels, medications, and the most recent blood gas variables, were recorded at the start of the study. SpO_2, heart rate (HR), respiratory rate (RR), and transcutaneous carbon dioxide (Tc_{CO2}) (if skin condition permitted) were continuously monitored (IntelliVue MP80 Monitor; Philips, Eindhoven, The Netherlands) and recorded at 12-second intervals. Transcutaneous oxygen tension was not measured. FiO_2 was documented at each CDP. Airway pressure (P_{aw}) was simultaneously measured from the ventilator. Esophageal pressure (P_{oes}) (SmartCath Esophageal Pressure Monitor; Viasys Healthcare, Palm Springs, California) was measured as a proxy for intrapleural pressure (P_{tp}) using the Bicore II (Cardinal Health, Hoechberg, Germany).

The balloon catheter was positioned in the lower esophagus and 0.5-0.6 mL of air was injected. At each CDP step, the volume of air in the balloon was aspirated and replaced to ensure that the balloon was within its working range. The catheter was maneuvered until a reproducible negative waveform during inspiration free of cardiac artifact was produced. Data were recorded at 200 Hz using LabChart 7 for Windows (AD Instruments, Sydney, Australia). Relative impedance change in end-expiratory thoracic volume ($\Delta ZEEV$) and tidal volume (ΔZV_T) were measured using electrical impedance tomography (EIT; GoeMF II EIT System; Cardinal Health, Hoechberg, Germany) sampling at 25 Hz as described previously.[24]

Baseline CDP was determined by the treating clinician. Following a 20-minute period at baseline CDP, the CDP was adjusted every 20 minutes to ensure volume stability[9,13] in the order 5-8-10-8 cm H_2O-baseline CDP, to determine whether a quasi-static P-V relationship could be described. During the last 6 minutes at each CDP, 3 2-minute recordings were made. FiO_2 was titrated to maintain SpO_2 at 88%-92%.

Statistical Analyses

EIT and P_{tp} recordings were reviewed to determine regions free from movement artifact. The last artifact-free 30-second period of stable EIT data at each CDP were analyzed. Shorter periods of stable data were analyzed if any EIT signals were unstable; however, because HR, RR, SpO_2, and Tc_{CO2} data were recorded at 12-second intervals, all of these data during the 2-minute epoch from which the artifact-free 30-second period of EIT data were extracted were analyzed. Data were compared across 6 phases: baseline; CDP_5, at CDP 5 cmH_2O; CDP_8 and CDP_{10}, after increasing to CDP 8 and 10 cmH_2O, respectively; CDP_{8R}, after decreasing to CPAP 8 cmH_2O; and CDP_{BaseR}, on returning to baseline CDP.

P_{tp} (cmH_2O) was calculated as (P_{aw} - P_{oes}) at end-expiration.[25] Transmission of positive airway pressure to the intrapleural space was determined (P_{oes}/P_{aw}) and expressed as a percentage of P_{aw}.[26] EIT data were analyzed offline using proprietary software (AUSPEX version 1.5; Cardinal Health, Hoechberg, Germany), as described previously.[24,27] Relative $\Delta ZEEV$ and ΔZV_T were determined in the entire cross-sectional slice-imaged (global), nondependent, and dependent hemithoraces during the 6 phases.

$\Delta ZEEV$ (in arbitrary units [AU]) was determined from the trough of the time course signals at each phase and referenced to CDP_5. Functional EIT (fEIT) images of the standard deviation of the impedance time course signal during each phase within 32 equal slices of the chest cross-sectional image were generated to determine ΔZV_T,[28,29] and the geometric center of ventilation[29,30] and tidal volume (V_T) within the middle, most dependent, and least nondependent gravity-distributed thirds of the chest were calculated.[28,29]

Because the true regional distribution of $\Delta ZEEV$ and ΔZV_T was unknown, a convenience sample of 20 infants was