Effect of Nasal Continuous and Biphasic Positive Airway Pressure on Lung Volume in Preterm Infants

Martijn Miedema, MD, PhD[1], Pauline S. van der Burg, MD[1], Sabine Beuger, MD[1], Frans H. de Jongh, PhD[1], Inez Frerichs, MD, PhD[2], and Anton H. van Kaam, MD, PhD[1]

Objective To monitor regional changes in end-expiratory lung volume (EELV), tidal volumes, and their ventilation distribution during different levels of nasal continuous positive airway pressure (nCPAP) and nasal biphasic positive airway pressure (BiPAP) in stable preterm infants.

Study design By using electrical impedance tomography and respiratory inductive plethysmography, we measured changes in EELV and tidal volumes in 22 preterm infants (gestational age 29.7 ± 1.5 weeks) during 3 nCPAP levels (2, 4, and 6 cmH_2O) and unsynchronized BiPAP (nCPAP = 6 cmH_2O; pressure amplitude = 3 cmH_2O; frequency = 50/min; inspiration time = 0.5 seconds) at 10-minute intervals. We assessed the distribution of these volumes in ventral and dorsal chest regions by using electrical impedance tomography.

Results EELV increased with increasing nCPAP with no difference between the ventral and dorsal lung regions. Tidal volume also increased, and a decrease in phase angle and respiratory rate was noted by respiratory induction plethysmography. At the regional level, electrical impedance tomography data showed a more dorsally oriented ventilation distribution. BiPAP resulted in a small increase in EELV but without changes in tidal volume or its regional distribution.

Conclusion Increasing nCPAP in the range of 2 to 6 cmH_2O results in a homogeneous increase in EELV and an increase in tidal volume in preterm infants with a more physiologic ventilation distribution. Unsynchronized BiPAP does not improve tidal volume compared with nCPAP. *(J Pediatr 2013;162:691-7)*.

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Nasal continuous positive airway pressure (nCPAP) is one of the most frequently used modes of respiratory support in preterm infants.[1] Its main physiologic effects on the preterm lung are a decrease in airway resistance and a pressure-dependent increase of the often-compromised end-expiratory lung volume (EELV).[2,3] As a result, preterm infants on nCPAP expend less effort breathing, have less paradoxical breathing, less apnea, and have improved gas exchange.[3-8] nCPAP is also considered a lung-protective mode of respiratory support because it reduces the need for invasive mechanical ventilation, which can cause secondary lung injury leading to bronchopulmonary dysplasia.[9] Regional overdistension and atelectasis caused by a heterogeneous distribution of aeration and ventilation are considered important pathways in the development of ventilator-induced lung injury.[10,11] However, in recent randomized controlled trials investigators failed to show a clear benefit of (early) nCPAP over invasive mechanical ventilation in terms of lung injury in preterm infants, which raises the question whether the increase in EELV during nCPAP is homogeneously distributed across the lung.

Those infants who do not respond to nCPAP are increasingly treated with nasal intermittent positive pressure ventilation (NIPPV). Studies have shown that, compared with nCPAP, NIPPV is more effective in the treatment of apnea and reduces extubation failure.[12,13] However, the underlying mechanisms of these beneficial effects are not well understood. Studies of tidal volume during NIPPV have shown conflicting results, with authors reporting increased and no change in tidal volumes.[14-18] To date, in no study have authors investigated the changes in EELV and the distribution of ventilation during NIPPV.

Electrical impedance tomography is a relatively novel, noninvasive, bedside monitoring technique capable of continuously measuring regional changes in lung impedance in a cross-sectional slice of the chest. These changes are highly correlated with actual intrathoracic air and ventilation changes.[19,20] In the present study, we used electrical impedance tomography to monitor

BiPAP	Biphasic positive airway pressure
CPAP	Continuous positive airway pressure
EELV	End-expiratory lung volume
FiO_2	Fraction of inspired oxygen
I:E	Inspiration-to-expiration time ratio
nCPAP	Nasal continuous positive airway pressure
NIPPV	Nasal intermittent positive pressure ventilation
$TcPCO_2$	Transcutaneous partial carbon dioxide pressure
$TcPO_2$	Transcutaneous partial oxygen pressure

From the [1]Department of Neonatology, Emma Children's Hospital, Academic Medical Center, Amsterdam, The Netherlands; and [2]Department of Anesthesiology and Intensive Care Medicine, University Medical Center Schleswig-Holstein, Campus Kiel, Germany

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regional changes in EELV and ventilation during different levels of nCPAP and nasal biphasic positive airway pressure (BiPAP) in stable preterm infants. In addition to electrical impedance tomography, lung volume changes also were monitored by respiratory inductance plethysmography, which provides information on global lung volume changes and was used in most previous studies on nCPAP and NIPPV. We hypothesized that increasing nCPAP would lead to a homogeneous increase in both EELV and ventilation and that adding BiPAP would not change this finding.

Methods

The study was performed in the neonatal intensive care unit of the Emma Children's Hospital, Academic Medical Center, Amsterdam, The Netherlands. The study was approved by the central committee on research involving human subjects, and written informed consent was obtained from both parents. Infants born at less than 32 weeks of gestation and who were younger than 7 days of age were eligible for enrollment if they were treated with nCPAP and were clinically stable (fraction of inspired oxygen [FiO_2] <0.30 and on average less than one instance of apnea [per 2 hours]). Exclusion criteria were congenital anomalies of the chest and/or abdomen and fragile skin condition. The patients were not sedated, and they were studied in the supine position.

Sixteen hand-trimmed ECG electrodes (Blue Sensor, BRS-50-K; Ambu, Inc, Linthicum Heights, Maryland) were equidistantly placed on the thorax circumference of the newborn just above the nipple line and connected to the Goettingen Goe-MF II electrical impedance tomography system (CareFusion, Hoechberg, Germany). Repetitive electrical currents (5 mA_{rms}, 100 kHz) were injected in rotation (scan rate 13 Hz) through adjacent electrodes pairs and voltage changes were measured by all other passive electrodes pairs. A back-projection image reconstruction algorithm generated a 32 × 32 matrix of local relative impedance changes (delta Z) compared with a reference state. Continuous online recording of impedance changes and continuous positive airway pressure (CPAP) pressures were performed with the use of Veit software (CareFusion).

Respiratory induction plethysmography bands were secured around the chest and abdomen of the infants and connected to a BiCore II system (Carefusion, Yorba Linda, California). Volume and pressure changes were continuously recorded during the study protocol with the use of Polybench software version 2.5.1 (Applied Biosignals GmbH, Weener, Germany). Calibration was performed with the previously described qualitative diagnostic calibration method via the use of a minimum of 20 consecutive breaths at 2 cmH_2O of nCPAP.[21]

nCPAP was delivered in all infants with the Infant Flow SiPAP system (CareFusion). The protocol consisted of 3 consecutive phases. During the first phase, the nCPAP pressure was set at 2 cmH_2O in all patients to standardize lung volume as much as possible. Next, nCPAP pressure was, in random order, increased to 4 and 6 cmH_2O at 10-minute intervals. At the beginning of the second phase, the CPAP pressure was set at 6 cmH_2O because in daily clinical practice BiPAP usually is applied during greater nCPAP levels. After a 10-minute stabilization period, unsynchronized BiPAP was started with the maximum pressure difference of 3 cmH_2O at a frequency of 50 breaths per minute with an inspiration time of 0.5 seconds. Patients were kept on BiPAP for 10 minutes and were then switched back to nCPAP for another 10 minutes. The third phase was similar to the second one, but this time BiPAP was synchronized by the use of an abdominal pneumatic capsule (Graseby Medical, Watford, United Kingdom). If an increase in FiO_2 or number of apneas was observed during the study protocol, the interventions were stopped and original settings were restored.

Data Acquisition and Analyses

EELV. Electrical impedance tomography data were analyzed offline with the use of AUSPEX version 1.6 (VUMC, Amsterdam, The Netherlands). The change in EELV was calculated by selecting a stable 30-second reference period at the start of each phase of the study protocol. All subsequent impedance recordings in each phase were referenced to this initial recording. Next, the relative change in EELV was calculated at CPAP 4 and 6 cmH_2O (phase 1) and before, during and after BiPAP (phases 2 and 3) by averaging the relative delta Z at the troughs of the spontaneous breaths in a stable 30-second recording period taken at the end of each 10-minute interval for each individual patient. This end-expiratory delta Z was then normalized for body weight. This analysis was performed for the whole cross section of the chest and for the ventral and dorsal halves of the scan area.

The calibrated respiratory induction plethysmography data were analyzed with a custom-built Polybench software package via the use of a similar approach and the same time periods as the electrical impedance tomography analysis. Analyses were conducted for the sum, ribcage, and abdominal signals separately.

Tidal Ventilation. To assess the change in tidal volume of the spontaneous breaths, each selected 30-second electrical impedance tomography period was then referenced to the average delta Z in that same period. Next, the delta Z signals were band pass-filtered in the band of spontaneous breathing frequency (10/min below the actual breathing frequency and 10/min above its second harmonic). By selecting the peaks and troughs, we were able to calculate, average, and then normalize the amplitudes for body weight.

To assess the regional distribution of the spontaneous breaths during each used pressure level of the study protocol, functional electrical impedance tomography images were generated by the use of the SD of the impedance time course of each individual pixel within the 32 × 32 matrix and normalized in each pixel.[20,22] In the anteroposterior ventilation profile, the impedance change was averaged for each slice and plotted. Next, the area under the curve for the ventral (slice 1-16) and dorsal lung region (slice 17-21) was