Tidal Volumes in Spontaneously Breathing Preterm Infants Supported with Continuous Positive Airway Pressure

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Objective To describe changes in tidal volume (V_T) and their correlation to changes in oxygen saturation and heart rate in spontaneously breathing preterm infants immediately after birth.

Study design In this prospective observational, 2-center study, a flow sensor was attached to the facemask of spontaneously breathing infants born at <37 weeks' gestational age who received continuous positive airway pressure (CPAP) immediately after birth. Respiratory function, heart rate, and oxygen saturation were continuously recorded during spontaneous breathing.

Results Fifty-five infants (mean [SD] gestational age 31 [26-36] weeks and birth weight 1647 [500] g) received mask CPAP in the delivery room. CPAP was started at a median (IQR) 90 (60-118) seconds after birth and was delivered for 720 (300-900) seconds. Median V_T ranged between 4.2 and 5.8 mL/kg with the individual V_T varied between 0.9 and 19.8 mL/kg. Overall, V_T increased over the first few minutes after birth and decreased thereafter. The increase in saturation after birth lagged behind the published normal ranges for spontaneously breathing preterm infants without CPAP.

Conclusions The 50th percentile for spontaneous V_T in preterm infants during mask CPAP ranged from 4.2 to 5.8 mL/kg, with wide individual variation observed in the first minutes after birth. Preterm infants requiring CPAP after birth may take longer to achieve so-called "normal" saturation targets. *(J Pediatr 2014;165:702-6)*.

Before birth, the airways and lungs are liquid-filled and the lungs take no part in gas exchange.[1] At birth, lung liquid has to be cleared from the airways to allow the entry of air and the establishment of a functional residual capacity.[1] The first breaths clear lung liquid, establish a functional residual capacity, and initiate spontaneous breathing while facilitating gas exchange.[2] O'Donnell et al[3] reported that the majority of preterm infants breathe and cry immediately after birth; however, approximately 10% of preterm infants require breathing assistance at birth.[4] There is increasing evidence that tidal volume (V_T) delivery rather than pressure should be monitored during positive pressure ventilation in the delivery room.[5-9] Although several studies reported V_T in spontaneously breathing preterm infants,[10-13] reference ranges of V_T over the first minutes after birth have not been established. The aim of this study was to describe the V_T reference range of preterm infants receiving continuous positive airway pressure (CPAP) via facemask and their correlation to changes in oxygen saturation (SpO_2) and heart rate (HR) in the first 15 minutes after birth.

Methods

This 2-center, observational study was carried out at the Royal Alexandra Hospital, Edmonton, Canada, and the Medical University of Graz, Austria, which are tertiary perinatal. The Royal Alexandra Hospital Research Committee and Health Ethics Research Board, University of Alberta and the Health Ethics Research Board, Medical University of Graz approved the study with parental consents. In Edmonton, infants (n = 38) were included between March 2013 and June 2013 and in Graz (n = 17) between January 2012 and June 2013. Deliveries of preterm infants were attended by the research team, which was not involved in the clinical care of the infants. Indication to start CPAP was decided by clinical team.

Ventilation Device and Facemask

All infants received CPAP via a round silicone facemask (ø35 mm or ø42 mm; Fisher & Paykel Healthcare, Auckland, New Zealand). Respiratory support was provided in both centers with a T-piece device (Giraffe Warmer; GE Health Care, Buckinghamshire, United Kingdom) a continuous-flow, pressure-limited device with a built-in manometer and a

CPAP	Continuous positive airway pressure
FiO_2	Fraction of inspired oxygen
HR	Heart rate
PEEP	Positive end-expiratory pressure
SpO_2	Oxygen saturation
V_T	Tidal volume

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G.S. is supported by the Canadian Institutes of Health Research (Banting Postdoctoral Fellowship) and Alberta Innovates (Health Solutions Clinical Fellowship). The authors declare no conflicts of interest.

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http://dx.doi.org/10.1016/j.jpeds.2014.06.047

positive end-expiratory pressure (PEEP) valve. The default settings used were a gas flow of 8 L/min and PEEP of 6 cm H_2O. At the discretion of the clinical team PEEP could be adjusted between 6 and 8 cm H_2O.

Study Monitoring Systems

An IntelliVue MP50 (Philips Healthcare, Philips Electronics Ltd., Markham, Ontario, Canada) was used in both centers to continuously measure HR, SpO_2, and blood pressure. HR was measured by the use of 3 Micro-Premie Leads (Vermed Inc, Bellows Falls, Vermont). A Masimo radical pulse oximeter (Masimo Corporation, Irvine, California) probe set at maximum sensitivity and 2-second averaging was placed around the infant's right wrist to measure percutaneous SpO_2.

Respiratory Function Monitoring

At the Royal Alexandra Hospital, a respiratory profile monitor (NM3; Philips Healthcare, Electronics Ltd, Markham, Ontario, Canada) was used to continuously measure V_T, airway pressures, and gas flow. Airway pressure and gas flow were measured by the use of a fixed orifice differential pressure pneumotachometer. V_T was calculated by integrating the flow signal. At the Medical University of Graz, a hot-wire anemometer flow sensor (Florian Respiratory Function Monitor, Acutronic Medical Systems AG, Zug, Switzerland) was used. In both centers, the flow sensor was placed between the T-piece and the facemask. In the delivery room, neither the respiratory function monitor nor the computer screen was visible to the resuscitation team and the monitor's alarm was disabled.

Data Analyses

All variables were stored continuously in a multichannel system "alpha-trace digital MM" (B.E.S.T. Medical Systems, Wien, Austria) for subsequent analysis. If infants required intermittent positive pressure ventilation at any stage during stabilization, they were excluded from analysis. A breath-by-breath analysis was performed manually for the duration of CPAP via facemask in each infant. PEEP, respiratory rate, and V_T were measured continuously. Mask leak was calculated from the mask by expressing the volume of gas that did not return through the flow sensor during expiration as a percentage of the volume that passed through the flow sensor during inspiration.[14] Mask leak was corrected for body temperature, pressure, and water vapor saturation using a standardized equation.

We used a thermo hygrometer to measure the temperature and humidity content of the inspired and expired resuscitation gas during a period of 1 week and averaged the values. These measurements were used to calculate the correction factor. Spontaneous breaths with a mask leak >30% were excluded from further analysis as these could underestimate the expired V_T measured. The data are presented as mean (±SD) for normally distributed continuous variables and median (IQR) when the distribution was skewed. The percentiles (10th, 25th, 50th, 75th, and 90th) for V_T were calculated by using the LMS-method described by Cole and Green and were fitted by using LMSchartmaker Version 2.54, a program to calculate age-related reference percentiles (Pan H, Cole TJ, 2011. Institute of Child Health, London, England; http://www.healthforallchildren.co.uk/).[15]

A linear mixed model with a first-order autoregressive covariance structure was used for calculation of overall effects and differences between groups at each minute. Subgroup analysis was performed to compare V_T in infants 26^{+0}-29^{+6} weeks' vs 30^{+0}-36^{+6} weeks' postmenstrual age by the use of the Mann-Whitney *U* test. *P*-values were 2-sided, and $P < .05$ was considered statistically significant. The mean and SD V_T for each minute was calculated and compared by the use of repeated-measures ANOVA with Tukey multiple comparison post-test analysis. Statistical analyses were performed with Stata (Intercooled 10; StataCorp, College Station, Texas).

Results

During the study period, a total of 120 preterm infants required respiratory support by mask: 65 required mask ventilation and 55 infants were treated with CPAP alone and were eligible for inclusion. Infant demographics are presented in **Table I**. Mask CPAP was started at a median of 90 (60-118) seconds after birth and delivered for a duration of 720 (300-900) seconds. A total of 12 065 breaths with 186 (154-316) breaths per infants were analyzed. A total of 2824 breaths were excluded because of mask leak >30%. None of the infants received positive pressure ventilation, intubation, chest compressions, or epinephrine in the delivery room. All infants were admitted to the neonatal intensive care unit supported on CPAP.

Respiratory Variables

The PEEP during mask CPAP was 6.2 (4.7-7.2) cm H_2O. The expired V_T in mL/kg is presented in **Figure 1** and **Table II**. Overall, the 50th percentile of spontaneous V_T was between 4 and 5 mL/kg. In addition, a V_T frequency analysis showed similar V_T for each minute throughout the 15-minute observation period. The overall respiratory rate was 39 (28-51) breaths per minute with an inspiration time of 0.4 (0.3-0.6) seconds. Respiratory rate and minute ventilation by minute are presented in **Table I**.

Table I. Infant characteristics

	n = 55
Gestation, wk*	31 (26-36)
Birth weight, g†	1647 ± 500
Male	25 (45)
Cesarean delivery	36 (78)
Full course of antenatal steroids	31 (82)
Delayed cord clamping	12 (22)
Apgar score at 1 minute‡	7 (6-8)
Apgar score at 5 minutes‡	8 (8-9)

Values are numbers (percentage) unless indicated.
*Mean (range).
†Mean ± SD.
‡Median (IQR).

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