



## Effects of a Sustained Inflation in Preterm Infants at Birth

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**Objective** To assess the clinical effect of an initial sustained inflation of 10 seconds and 25 cmH<sub>2</sub>O in preterm infants at birth.

**Study design** In this observational study inflation pressures and tidal volumes were recorded with the use of respiratory function monitoring of preterm infants <32 weeks' gestation receiving a sustained inflation. Inspiratory tidal volume (V<sub>ti</sub>) and expiratory tidal volume (V<sub>te</sub>) of sustained inflation and cumulative V<sub>ti</sub> and V<sub>te</sub> of breaths during sustained inflation were determined. Heart rate and oxygen saturation were measured before and after the sustained inflation.

**Results** Seventy infants were included (median [IQR]: gestational age 29 [27-30] weeks). Mean (SD) sustained inflation duration was 10.5 seconds (2.9 seconds) with positive inflation pressure 24.2 cmH<sub>2</sub>O (2.3 cmH<sub>2</sub>O) and positive end-expiratory pressure 6.0 cmH<sub>2</sub>O (1.8 cmH<sub>2</sub>O). In 20 of 70 infants, no volumes were delivered during the sustained inflation because of mask leak. No leak occurred in 50 of 70 infants, of whom 36 of 50 breathed during the sustained inflation. In 14 of the infants who did not breathe, V<sub>ti</sub> and V<sub>te</sub> were 0.9 mL/kg (0.4-2.7 mL/kg) and 0.6 mL/kg (0.1-2.0 mL/kg) with a functional residual capacity (FRC) gain of 0.0 (−0.5 to 0.6) mL/kg. In 36 of 50 infants who breathed during the sustained inflation, V<sub>ti</sub> was 2.9 mL/kg (0.9-9.2 mL/kg) and V<sub>te</sub> 3.8 mL/kg (1.0-5.9 mL/kg), whereas cumulative V<sub>ti</sub> of breaths was 16.4 mL/kg (6.8-23.3 mL/kg) and cumulative V<sub>te</sub> of breaths was 5.8 mL/kg (1.2-16.8 mL/kg) with an FRC gain of 7.1 mL/kg (1.7-15.9 mL/kg). Heart rate and oxygen saturation did not increase immediately after the sustained inflation.

**Conclusions** A sustained inflation of 10 seconds and 25 cmH<sub>2</sub>O in preterm infants at birth was not effective unless infants breathed. Although large mask leak accounted for approximately one-third of failures, as FRC gain was only associated with breathing, we speculate that active glottic adduction may be responsible for most failures. (*J Pediatr* 2014;165:903-8).

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Many preterm infants need positive pressure ventilation (PPV) to aerate their lungs after birth to overcome the high surface tension and frictional forces caused by liquid-filled airways.<sup>1</sup> An initial sustained inflation may improve lung aeration and functional residual capacity (FRC) during the resuscitation of preterm infants at birth.<sup>2,3</sup> During a sustained inflation, a positive inflation pressure (PIP) is administered for a prolonged period, which allows time for the air/liquid interface to move into the distal airways.<sup>4</sup>

Studies performed in preterm rabbit pups with simultaneous phase-contrast radiograph imaging and plethysmography have shown that an initial sustained inflation immediately after birth provided more uniform lung aeration, larger FRC, and more consistent tidal volumes than regular PPV.<sup>4,5</sup> An experimental study using sustained inflation of 20 seconds for the resuscitation of asphyxiated lambs improved respiratory and hemodynamic function, causing a prompt increase in heart rate (HR) after the sustained inflation was applied.<sup>6</sup> Although clinical studies reported less need for intubation, mechanical ventilation and bronchopulmonary dysplasia when a sustained inflation was applied at birth,<sup>7-10</sup> the clinical effect in preterm infants remains uncertain.

The effect of the initial PPV at birth is largely dependent on effective mask technique, but this can be difficult to achieve.<sup>11-15</sup> Most clinicians are not aware of mask leak, airway obstruction, and the occurrence of inadvertent high peak pressures.<sup>12,16,17</sup> We recently measured the effect of mask ventilation in preterm

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FRC	Functional residual capacity
HR	Heart rate
PIP	Positive inflation pressure
PPV	Positive pressure ventilation
SpO <sub>2</sub>	Oxygen saturation
V <sub>te</sub>	Expired tidal volume
V <sub>ti</sub>	Inspired tidal volume

infants at birth by using respiratory function monitoring and often observed inadequate low tidal volumes and large mask leak.<sup>18</sup> We also reported that spontaneous breathing during PPV frequently occurred.<sup>18</sup>

In experiments on animals, a sustained inflation improved lung function without adverse circulatory effects and positively affected cerebral oxygenation.<sup>19</sup> A recent trial in preterm infants showed beneficial effects of a ventilation strategy that incorporated a sustained inflation of 10 seconds.<sup>10</sup> We recently reported the respiratory function measurements of 5 initial inflations of 2-3 seconds,<sup>18</sup> but the direct effect of a 10-second sustained inflation has not been investigated in infants. When leak occurs during the sustained inflation, gas flow remains positive for a prolonged period, and a supraphysiological inspired tidal volume (V<sub>ti</sub>) will be measured; however, because very little volume entered the airways, the expired tidal volume (V<sub>te</sub>) is very low. In the absence of mask leak, low inspired volumes also occur when the mask obstructs the mouth and nose, secretions block the oropharynx, the glottis is closed, or the PIP is not high enough to overcome the frictional resistance of moving the air-liquid interface distally. The aim of this observational study was to investigate the clinical effect of a sustained inflation during initial respiratory support in preterm infants at birth by measuring clinical variables and lung function.

## Methods

The local institutional review boards of the Leiden University Medical Center approved physiologic and video recordings at birth in the delivery room when respiratory support was expected. Recordings are performed as a standard of care in our unit. The data for this observational study were prospectively collected for audit, teaching, and research purposes with written parental consent after birth.

Respiratory support was delivered with a T-piece resuscitator (Neopuff, Fisher & Paykel, Wellington, New Zealand) and a properly sized round face mask (35-mm face mask; Fisher & Paykel, Wellington, New Zealand, or size 0/0 or 0/1 face mask; Laerdal, Stavanger, Norway). Since 2010, our local resuscitation guidelines deviated from the national guidelines by recommending to start respiratory support (PPV or continuous positive airway pressure) in preterm infants (<32 weeks' gestational age) with an initial sustained inflation of 10 seconds using a PIP of 25 cmH<sub>2</sub>O and a positive end-expiratory pressure of 5 cmH<sub>2</sub>O with a fractional inspired oxygen of 0.3. Respiratory support was given if the infant was apneic (PPV), had labored breathing (continuous positive airway pressure), and/or the HR was less than 100 beats per minute.

Physiologic and video recordings were performed in preterm infants if there was time to set up the equipment. The use of a respiratory function monitor (Acutronic Medical Systems AG, Hirzel, Switzerland), a pulse oximeter (Masimo Radical 7, Masimo Corporation, Irvine, California), and Spectra program (Spectra, Grove Medical Limited, Hampton, United Kingdom) for physiologic recordings has been

described in detail in a previous publication.<sup>18</sup> According to the manufacturer, the Florian respiratory function monitor is able to measure accurately down to 90 mL/min (1.5 mL/s).<sup>20</sup> However, to determine the accuracy of the Florian, we performed a bench study using a gas flow analyzer (Biotek Instruments, Winooski, Vermont) and observed the following: (1) gas flow could be measured accurately down to a gas flow of 50 mL/min (0.8 mL/s); (2) <50 mL/min gas flow was measured, but values became inaccurate; and (3) when gas flow was stopped, the Florian accurately showed zero flow. The hot-wire anemometers are capable of accurately measuring even lower gas flows.<sup>21,22</sup>

Recordings were reviewed from infants born between 2009 and 2013. Recordings were made of infants who were expected to need respiratory support born <32 weeks of gestational age, without congenital malformations regardless if prenatal steroids were administered or oligo- or anhydramnios existed. Recordings were analyzed only when a face mask was used for the administration of the initial sustained inflation.

V<sub>ti</sub>, V<sub>te</sub>, and cumulative V<sub>ti</sub> and V<sub>te</sub> of spontaneous breaths during the sustained inflation were determined. When during a sustained inflation breathing occurred, V<sub>ti</sub> and V<sub>te</sub> were determined at the plateau level before the breath. Leak (%) was calculated using the formula  $([V_{ti} - V_{te}]/V_{ti}) \times 100$ . When little mask leak occurred, tidal volumes and gain in FRC could be calculated. In this case flow goes back to zero soon after commencing the sustained inflation when the passive inflation has ended. FRC gain was calculated by subtracting total expiratory volume from inspiratory volume. HR and oxygen saturation (SpO<sub>2</sub>) were determined directly before and after the sustained inflation and 30 and 60 seconds after the sustained inflation using a pulse oximeter (Masimo Radical 7, Masimo Corporation, Irvine, California).

As described in previous clinical<sup>3,8-10</sup> and experimental studies,<sup>4,5,19</sup> the pulmonary effects of an effective sustained inflation would be characterized by a volume that increases during a prolonged period of PIP. The gas flow will be characterized by a peak positive flow at the start, followed by slower positive gas flow reflecting airway recruitment caused by the liquid-air interface moving distally and creating a FRC. Because the flow wave characteristics of face mask leak are similar to FRC recruitment, it is difficult to differentiate effect of the sustained inflation on FRC from mask leak. However, when mask leak occurs during a sustained inflation with a flow of 8-10 L/min, a continuous leak with high gas flows is observed. Thus, when the measured V<sub>ti</sub> was supraphysiological (greater than the total lung capacity of approximately 60 mL/kg) and the V<sub>te</sub> was small, this was deemed to be attributable to mask leak.

The flow returns to zero immediately after the initial positive peak in flow at the start of the sustained inflation. This reflects that no mask leak occurred, but also little or no movement of the liquid-air interface recruiting the airways. The appearance of spontaneous breaths can be identified during the sustained inflation by the presence or absence of

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