Intrapulmonary Volume Changes during Hiccups versus Spontaneous Breaths in a Preterm Infant

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Established Facts

- Hiccups occur at all ages but are most common during fetal development.
- Hiccups are induced by a wide variety of stimuli and they are unlikely to have a respiratory origin.

Novel Insights

- Hiccups mostly occurred during the expiratory phase of breathing and were associated with a shorter inspiratory time and a larger tidal volume compared with spontaneous breaths.
- Volume changes during hiccups were mainly restricted to the larger airways but some gas flow also reached the lung parenchyma.

Keywords

Electrical impedance tomography · Hiccup · Preterm infant

Abstract

Hiccups occur at all ages but are most common during fetal development, and accordingly, they are seen regularly in preterm infants. However, the physiologic correlate of hiccups has never been established. We present the case of a preterm infant who developed a spell of hiccups and compared lung volume changes during hiccups with spontaneous breaths using electrical impedance tomography. Hiccups mostly occurred during the expiratory phase of breathing and were associated with a shorter inspiratory time and a larger tidal volume compared with spontaneous breaths. The center of ventilation was shifted toward the ventral (non-gravity-dependent) part of the lung during hiccups and volume changes were mainly restricted to the larger airways, but some gas flow also reached the lung parenchyma. Our observations shed new light on this phenomenon, which is well known but little researched, and our findings may imply a physiological impact of hiccups during fetal development.

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Introduction

Hiccups primarily result from contraction of the diaphragm against a closed glottis, although the glottis eventually opens to allow the late and rapid influx of air. Hiccups are induced by a wide variety of stimuli and they are unlikely to have a respiratory origin [1]. They occur at all ages but are most common during fetal development, and accordingly, they are seen regularly in preterm infants [1, 2]. However, the physiologic correlate of hiccups has never been established. In this case report, we describe lung volume changes during a spell of hiccups in a preterm infant using electrical impedance tomography (EIT).

Case Report

During a randomized controlled trial (clinicaltrials.gov, Identifier: NCT04315636) investigating the effect of surfactant nebulization, we recorded EIT data at a frame rate of 51 Hz (LuMon\textsuperscript{TM}, SenTec AG, Landquart, Switzerland) in supine position at prespecified time points after birth. Written informed parental consent was obtained for trial participation and for this case report. Spontaneous breaths and hiccups were visually identified in the EIT raw signal and ventilation characteristics were extracted separately using Matlab (Mathworks, Nantick, MA, USA). We assessed and compared tidal volumes (V_{T-spont} and V_{T-Hiccup} i.e., difference in lung impedance between start and end of inspiration and hiccup, respectively), inspiratory time (T_{Spont} and T_{Hiccup}), regional distribution of tidal volumes in 36 horizontal slices, and the center of ventilation in the vertical (CoV_{V-D}) as well as the horizontal axis (CoV_{R-L}) [3, 4]. The CoV describes breath distribution, with higher percentages indicating a shift toward the dorsal and left lung, respectively [4]. Median values with interquartile ranges (IQR) are presented and comparisons were performed using a Wilcoxon test.

The infant was born via cesarean section due to pathological cardiocogram readings at 30 1/7 weeks gestation (birth weight 1,550 g; antenatal steroid prophylaxis completed). After birth, the infant was stabilized on continuous positive airway pressure (CPAP). The first chest X-ray was compatible with “wet lung” disease and a distended stomach was noted.

During a prespecified EIT follow-up recording 12 h after birth, the infant (in supine position, supported on nasal CPAP with a positive end-expiratory pressure of 6 cmH\textsubscript{2}O) developed hiccups. The entire hiccup spell lasted 758 s and we recorded 226 hiccups at variable intervals (hiccup rate: 18/min) and 405 spontaneous breaths during the same timeframe (respiratory rate: 32/min). Hiccups occurred more often during expiration (144 out of 226; 63.7%) than during inspiration (20/226; 8.8%) or between breaths (62/226, 27.4%). The infant’s ratio of inspiratory to expiratory time (I:E-ratio) was 1:3.

![Fig. 1. Lung volume changes during hiccups and spontaneous breaths. a Shows a 20-s extract of the original EIT recording. The EIT signal from single pixels within the thorax was then extracted: the signal changes over the trachea (red) and the right lung (green) are shown in panel (b\textsuperscript{1}, b\textsuperscript{2}), respectively. AU, arbitrary units; s, seconds.](image-url)
Hiccups led to a specific and repetitively identical signal of lung volume changes measured by EIT (Fig. 1a). There was less distal lung signal during hiccups, suggesting that most volume changes were limited to major airways and only some changes occurred within predefined lung regions (Fig. 1b). Compared to spontaneous breaths, hiccups were characterized by a larger tidal volume (median [IQR]: \( V_T \)-Hiccup 3.4 [3.1–3.8] AU/kg vs. \( V_T \)-Spont 1.9 [1.5–2.5] AU/kg, \( p = 0.007 \)) and a shorter inspiratory time (median [IQR]; Ti-Hiccup 138 [138–157] ms vs. Ti-Spont 433 [374–511] ms, \( p < 0.001 \)). There were pronounced differences in the distribution of lung volume changes between hiccups and spontaneous breaths (Fig. 2). Correspondingly, \( \text{CoV}_{V,D} \) was shifted toward the ventral (non-gravity-dependent) part of the lung during hiccups (median [IQR] \( \text{CoV}_{V,D}-\text{Hiccup} \) 47% [44–50] vs. \( \text{CoV}_{V,D}-\text{Spont} \) 63% [60–67], \( p < 0.001 \)) while the horizontal distribution was comparable (median [IQR]: \( \text{CoV}_{R,L}-\text{Hiccup} \) 44% [39–47] vs. \( \text{CoV}_{R,L}-\text{Spont} \) 44% [39–46], \( p = 0.33 \); Fig. 2).

**Discussion**

To our knowledge, we present the first description of intrapulmonary volume changes during a spell of hiccups in a preterm infant. Hiccups mostly occurred during the expiratory phase of breathing and were associated with a shorter Ti and a larger \( V_T \) compared with spontaneous breaths. Volume changes during hiccups were mainly restricted to the larger airways, but some gas flow also reached the lung parenchyma.

Descending excitatory input into the diaphragm from the respiratory center is more active during inspiration and relatively silent during expiration [5], which may explain why hiccups were more common during expiration.
This difference exceeded the infant’s I:E-ratio, thus making a spurious correlation unlikely. As mechanoreceptors in the esophagus and the proximal stomach are thought to be involved in the afferent limb of inducing hiccups [6], it is not surprising that the studied infant had a slightly distended stomach due to CPAP support.

In contrast to spontaneous breaths, the diaphragm contracts against a (partially) closed glottis during a hiccup which initially causes a large decrease in intrathoracic pressure and a subsequent rapid air entry into the lungs upon slight glottis opening [7]. In the studied infant, this is illustrated by the short Ti during hiccups and a sharp increase in intrathoracic gas volume, the magnitude of almost twice of a spontaneous VT. This finding is comparable to previous results in adults [8]. Lung recoil is then largely responsible for expelling this air and as the lung is relatively incompressible, the interruption to spontaneous breathing is minor.

Despite knowing the phenomenon for centuries, the understanding of the pathophysiology of hiccups is still very limited. Hiccups may be a dysfunction or lack of reciprocal inhibition between the inspiratory complex and the glottis closure complex and, as such, is thought to be non-respiratory in origin [7]. In fetuses and preterm infants, hiccups may provide afferent input into developing sensory cortices, thereby assisting in their maturation [9]. In this case report, we now saw that intrapulmonary volume changes during hiccups were mainly detectable in the major airways while only some of the hiccup volume reached the lung parenchyma, possibly due to the newborn’s highly compliant chest wall and the short Ti of the hiccup.

Due to the viscosity of lung liquid, diaphragm contraction during fetal breathing movements results mainly in chest wall deformation and almost no change in lung volume [10]. Similarly, the chest wall is known to retract during large inspiratory efforts in newborn infants and, given the higher intrathoracic pressure during hiccups (indicated by the higher VT and shorter Ti), it is not surprising that air is mainly detectable in the major airways and, correspondingly, air distribution is shifted to the ventral regions of the lung. While findings are based on a single case and cannot be extrapolated as such, our observations still shed new light on this phenomenon, which is well-known but little researched. Finally, our findings may imply a physiological impact of hiccups during fetal development.

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Statement of Ethics

This study protocol was reviewed and approved by the Cantonal Ethics Committee of Zurich (approval number KEK-2020-00890) and prospectively registered on ClinicalTrials.gov (NCT04315636) on March 19, 2020. The parents provided written antenatal consent for participation in the original study and additional written informed consent for publication of this case report.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Vincent D. Gaertner analyzed the data and wrote the first draft of the manuscript. Andreas D. Waldmann extracted EIT data and helped analyze the data. Christoph M. Rüegger collected the data and supervised the project. All the authors (Vincent D. Gaertner, Andreas D. Waldmann, Stuart B. Hooper, Dirk Bassler, Christoph M. Rüegger) made substantial contributions to interpretation of the data. All the authors contributed to redrafting the manuscript and revising it critically for important intellectual input. All the authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement

Data are not publicly available as they are containing information that could compromise the privacy of the patient but are available from the corresponding author (V.D.G.) upon reasonable request.
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