

# Carbon Dioxide Levels When Starting High Frequency Ventilation in Neonates

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## Abstract

**Objective:** High-frequency ventilation (HFV) is an effective means to achieve gas exchange in neonates. Adequate carbon dioxide (pCO<sub>2</sub>) levels are best achieved immediately after starting HFV, avoiding either hypercapnia or hypocapnia. We aimed to determine the initial pCO<sub>2</sub> levels after starting HFV, and the time taken to obtain the initial blood gas. **Methods:** We conducted an observational retrospective study on neonates that required their first episode of HFV. Data included the first blood gas result after starting HFV and when the gas was taken after starting HFV. **Results:** This study included 112 neonates with a median birth weight of 938 (IQR: 692 - 1549) grams and gestational age of 27.2 (24.6 - 30.7) weeks. The first pCO<sub>2</sub> after starting HFV (mean (SD)) was 53.7 (22) mmHg. Of 112, 15 (13.4%) showed initial hypocapnia (pCO<sub>2</sub> < 35 mmHg), and 17 (15.2%) showed hypercapnia (pCO<sub>2</sub> > 65 mmHg)—a total of 28.6% unacceptable pCO<sub>2</sub> levels. Of 112, the first blood gas was obtained within 30 minutes in 47 (42%) and within one hour in 85 (76%), with a significant delay of two or more hours in eight (7.1%). **Conclusion:** Many neonates had unacceptable pCO<sub>2</sub> levels upon starting first-time HFV. There were significant delays in obtaining the initial gas.

## Keywords

Infant, Newborn, High-Frequency Ventilation, Carbon Dioxide

## 1. Introduction

One of the major problems when starting high-frequency ventilation (HFV) in neonates is knowing which amplitude can be set to achieve an acceptable pCO<sub>2</sub> level. Initial amplitude is usually set at a level that achieves adequate chest wiggle as assessed by the clinician.

Often the first pCO<sub>2</sub> level after starting HFV can be outside the acceptable range, which can be harmful. Hypocapnia causes cerebral vasoconstriction, decreased cerebral blood flow, cerebral ischaemia, and periventricular leukomalacia. Hypercapnia induces cerebral vasodilation with increased CBF increasing the risk for severe intraventricular haemorrhage. Both can lead to poor neurological outcomes for preterm infants. There is only anecdotal evidence available of how often the first pCO<sub>2</sub> level is outside acceptable values. Also, the first blood gas after starting HFV may not be done in a timely manner. The extent of these problems is unknown.

Our aims were to determine the initial pCO<sub>2</sub> levels that occurred after starting HFV, and the time taken to obtain the initial blood gas.

## 2. Methods

We conducted an observational service evaluation using a retrospective cohort of neonates that required their first HFV episode from 1 January 2017 to 31 March 2019 in the Grantley Stable Neonatal Unit at the Royal Brisbane and Women's Hospital.

In our unit HFV is generally started when high pressures are required to achieve adequate oxygenation despite a fraction of inspired oxygen > 80%, or large tidal volumes are required to achieve adequate CO<sub>2</sub> clearance, using conventional mechanical ventilation. This is regardless of gestational age or weight. After starting HFV a blood gas should be done within 30 minutes.

Data were collected on gestational age at birth, birth weight, sex, condition before starting HFV (post-natal age, post-menstrual age, lung disease, ventilation settings, last pCO<sub>2</sub> level, use of postnatal steroids prior to starting HFV), and initial HFV episode (reason for starting HFV, duration of HFV required, first blood gas result after starting HFV, initial ventilation settings on HFV).

Statistical analysis: Data were analysed using simple descriptive statistics presented as number (percent), mean (standard deviation—SD), or median (interquartile range—IQR) and was performed using Microsoft<sup>®</sup> Excel for Mac (version 16.25 (19051201), Product ID 02954-050-803041, Redmond, Washington, USA).

## 3. Results

A total of 112 neonates were included in the study. The median (IQR) birth weight was 938 (692 - 1549) grams, and the median (IQR) gestational age was 27.2 (24.6 - 30.7) weeks. Fifty-five percent (61/112) were male. Before starting HFV the median (IQR) FiO<sub>2</sub> was 0.55 (0.43 - 1.0); 97/112 (87%) were on conventional mechanical ventilation and in the remaining 15 (13%) HFV was the first mode of ventilation used. The mean (SD) pCO<sub>2</sub> prior to starting HFV was 61.7 (17.0) mmHg. The median (IQR) post-natal age at starting HFV was 0.61 (0.11 - 2.45) days.

After HFV started the initial ventilation used was as follows: mean (SD) am-

plitude of 21.3 (6.2) cmH<sub>2</sub>O; mean (SD) frequency of 13 (2.7) Hz; mean (SD) mean airway pressure (MAP) of 15.4 (2.8) cmH<sub>2</sub>O, and median (IQR) FiO<sub>2</sub> of 0.60 (0.35 - 1.0). The mean (SD) first pCO<sub>2</sub> after starting HFV was 53.7 (22) mmHg. The median (IQR) duration of HFV was 3.9 (1.1 - 10) days.

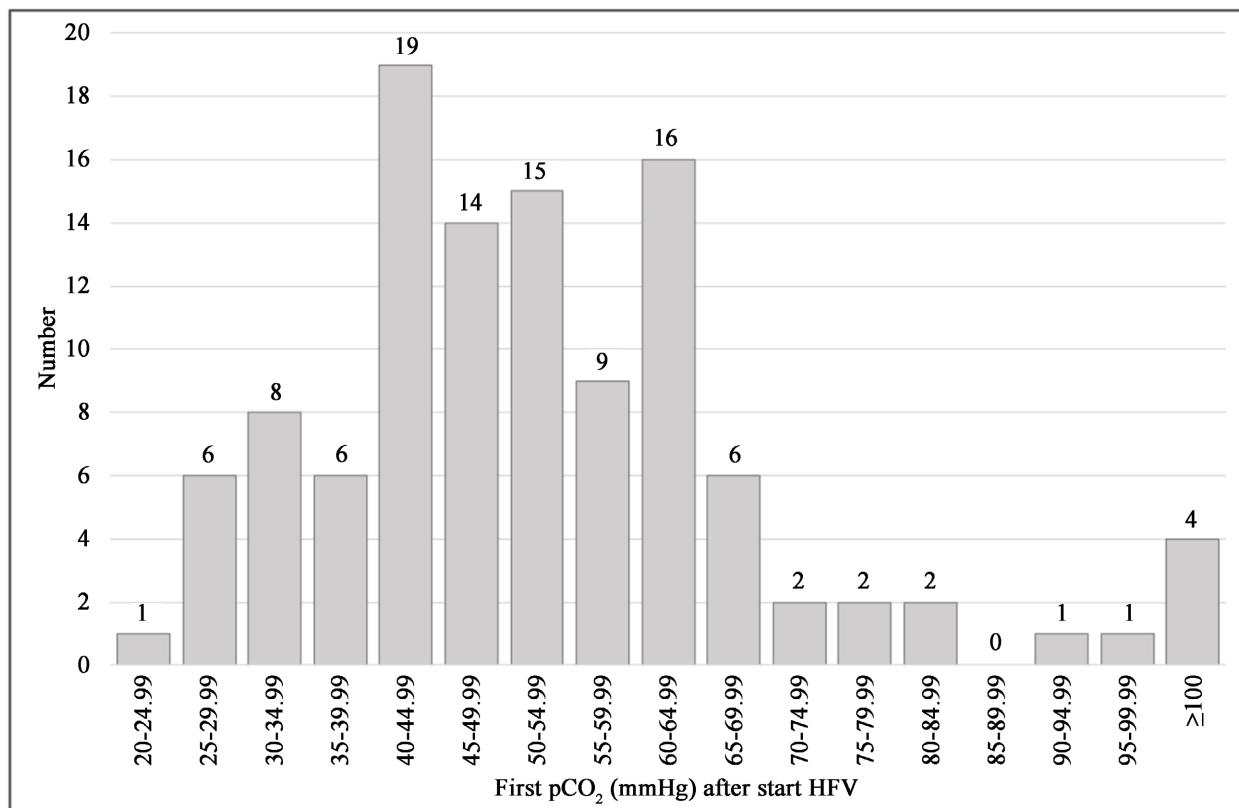
Of the 112 neonates started on HFV, the first blood gas results were obtained within 30 minutes in 47 neonates (42%) and within one hour in 85 neonates (76%), with a significant delay of two or more hours in eight (7.1%).

Thirty-two of the 112 initial pCO<sub>2</sub> levels (28.6%) were significantly hypo- or hypercapnic; 15 (13.4%) hypocapnic (pCO<sub>2</sub> < 35 mmHg), and 17 (15.2%) hypercapnic (pCO<sub>2</sub> > 65 mmHg). The frequency distribution of first pCO<sub>2</sub> level is shown in **Figure 1**.

#### 4. Discussion

We have demonstrated that a large proportion (29%) of neonates are either significantly hypocapnic (pCO<sub>2</sub> < 35 mmHg) or significantly hypercapnic (pCO<sub>2</sub> > 65 mmHg) when starting on HFV. There is also a significant delay in obtaining blood gas after starting HFV.

To our knowledge, this is the first study investigating the incidence of the initial pCO<sub>2</sub> levels after starting HFV. Our study not only highlights the problem of obtaining the initial pCO<sub>2</sub> level in a timely fashion, but also the resulting delays in reaching an acceptable pCO<sub>2</sub> level.



**Figure 1.** Frequency distribution of first pCO<sub>2</sub> level after starting HFV.

Ventilation (CO<sub>2</sub> clearance) during HFV happens predominantly by facilitated diffusion with CO<sub>2</sub> exchange mostly dependent on the set amplitude and frequency [1]. Evidence on how to optimise amplitude, other than the objective assessment of the amount of chest wiggle, is emerging by way of measuring and controlling tidal volume (VT<sub>hf</sub>) using volume guarantee (VG) and CO<sub>2</sub> diffusion coefficient (DCO<sub>2</sub>) levels [1] [2] [3] [4] [5]. Recent studies show that methods such as using VG can minimize the amount of time spent to achieve acceptable pCO<sub>2</sub> levels, better achieve pCO<sub>2</sub> levels in the target range and reduce fluctuations in pCO<sub>2</sub> levels [2]. To date the optimal DCO<sub>2</sub>, VT<sub>hf</sub> and VG values have not yet been established, with studies reporting on these parameters showing great variations between populations of infants, lung pathology, initial ventilator settings used (especially frequency), and targeted pCO<sub>2</sub> levels [1] [2] [3] [4] [5]. Nevertheless, there is enough data to enable a reasonable estimate of the tidal volume to target when starting HFV, as opposed to guessing the best amplitude to set based on an inaccurate assessment of chest wiggle.

The presence or absence of brain lesions (e.g. haemorrhage or ischaemia) will affect acceptable pCO<sub>2</sub> levels. Hypocapnia causes cerebral vasoconstriction, decreased cerebral blood flow, cerebral ischaemia, and periventricular leukomalacia. Hypercapnia induces cerebral vasodilation with increased CBF increasing the risk for severe intraventricular haemorrhage. Both can lead to poor neurological outcomes for preterm infants.

Implementing changes resulting from these findings to improve clinical practice will include early and more timely blood gas assessments and the use of VG when starting HFV (using an estimated targeted VT<sub>hf</sub> for a given frequency). We anticipate that this will lead to more initial pCO<sub>2</sub> levels in the target range and a shortened duration to achieve acceptable pCO<sub>2</sub> levels.

## 5. Conclusion

In conclusion, a large proportion of neonates have unacceptable pCO<sub>2</sub> levels values upon starting HFV for the first time. There are also significant delays in obtaining the initial pCO<sub>2</sub> levels.

## Acknowledgements

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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