

# Potential rebreathing of carbon dioxide during noninvasive ventilation provided by critical care ventilator

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AA Hussain, D Vines. Potential rebreathing of carbon dioxide during noninvasive ventilation provided by critical care ventilator. *Can J Respir Ther* 2022;58:111–114. doi: 10.29390/cjrt-2022-013.

**Background:** Critical care ventilators are frequently used to provide noninvasive ventilation (NIV) support to critically ill patients. Questions remain regarding carbon dioxide (CO<sub>2</sub>) clearance while using a critical care ventilator and dual limb circuit with various patient interfaces. The purpose of this study is to determine the positive end expiratory pressure (PEEP) level required to effectively washout CO<sub>2</sub> for full-face and oronasal masks when using a dual limb circuit.

**Method:** This randomized crossover trial was conducted at an academic medical center in the Midwest United States. After obtaining informed consent, eight healthy volunteers were placed on a 980 Puritan Bennett (Medtronic, Minneapolis, MN) ventilator operating in the NIV mode. All subjects performed 20 min of breathing on four levels of PEEP (0, 2, 4, and 5 cm H<sub>2</sub>O) and pressure support of 5 cm H<sub>2</sub>O. NIV settings were applied to four masks (two oronasal and two full-face masks) that were randomly selected with a 5-min washout period between each mask. The fraction of inspired carbon dioxide (F<sub>ICO<sub>2</sub></sub>) was sampled/monitored with a nasal cannula using a Capnostream 20p monitor (Medtronic, Minneapolis, MN) and reported as percentages. A Kruskal-Wallis test was used to reveal significant differences across PEEP levels. Pairwise comparisons of the groups were made using Mann-Whitney tests with a family-wise error correction.

**Results:** Median (IQR) F<sub>ICO<sub>2</sub></sub> was significantly lower 0.0% (0%–0.92%) at PEEP of 5 compared to 1.83% (0.66%–4.0%;  $p < 0.001$ ) at PEEP of 0 or 1.0% (0.33%–2.66%;  $p = 0.002$ ) at PEEP of 2. F<sub>ICO<sub>2</sub></sub> was significantly lower 0.5% (0%–1.92%) at PEEP of 4 compared to PEEP of 0 ( $p = 0.001$ ).

**Conclusion:** A PEEP level of at least 5 cm H<sub>2</sub>O associated with the reported leak was required to minimize the likelihood of CO<sub>2</sub> rebreathing while using a critical care ventilator to provide NIV with a double limb circuit and full-face or oronasal masks.

**Key Words:** carbon dioxide clearance; noninvasive ventilation; mechanical ventilation; CO<sub>2</sub> rebreathing; oronasal mask; full-face mask

## INTRODUCTION

Noninvasive ventilation (NIV) is widely used in managing critically ill patients ranging from Chronic Obstructive Pulmonary Disease (COPD) and pulmonary edema to hypoxemic respiratory failure and immunosuppression [1–4]. NIV can be delivered by a dedicated noninvasive ventilator that utilizes a single limb circuit requiring an expiratory port to allow for carbon dioxide (CO<sub>2</sub>) clearance [5]. NIV can also be delivered by critical care ventilators that utilize a dual limb circuit, although they may not function well with large leaks [5]. CO<sub>2</sub> rebreathing is a concern during NIV and may adversely affect patient tolerance with NIV [6].

Samolski et al. [7] studied the CO<sub>2</sub> rebreathing while using a single limb circuit. They assessed the effect of the expiratory port location at different sites using nasal and oronasal masks. They reported baseline pressure as low as 4 cm H<sub>2</sub>O was effective in preventing CO<sub>2</sub> rebreathing [7]. Another study reported CO<sub>2</sub> rebreathing might occur in NIV masks with lower intentional leak rates using normal volunteers [8]. Others compared full-face masks against oronasal masks in patients with acute respiratory failure. They found that full-face masks resulted in a lower venous P<sub>CO<sub>2</sub></sub> after the first 6 h [9]. These studies did not test different

expiratory positive airway pressures (EPAP) on CO<sub>2</sub> clearance using a critical care ventilator with a dual limb circuit.

A study that compared oronasal masks, full-face masks, and helmet in patients with acute hypercapnia respiratory failure using an EPAP of 3–5 cm H<sub>2</sub>O reported improved gas exchange, but CO<sub>2</sub> clearance from the masks were not assessed [10]. Currently there are no published manuscripts assessing CO<sub>2</sub> rebreathing or clearance of CO<sub>2</sub> from masks using a critical care ventilator with a double limb circuit to provide NIV.

The level of EPAP or positive end-expiratory pressure (PEEP) needed to washout CO<sub>2</sub> from the NIV masks remains undetermined when using a critical care ventilator. The alternative hypothesis of this study is that PEEP levels of 0 or 2 cm H<sub>2</sub>O would result in more CO<sub>2</sub> accumulating in the mask for full-face masks (FFM) and oronasal masks (ONM) compared to 4 or 5 cm H<sub>2</sub>O when using a critical care ventilator with a dual limb circuit in normal volunteers.

## METHODS

This randomized crossover pilot study was conducted between 13 July and 15 August 2018 after obtaining Rush University's (Chicago, IL)

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institutional review board approval. Normal volunteers (students, staff, or faculty) were recruited from the university. Volunteers were screened with inclusion and exclusion criteria. Study participants were included if they were healthy (absence of chronic disease or acute illness), had oxygen saturation more than 92%, and were older than 18 years of age. Study participants were excluded if they had a history of NIV use at all, facial surgery or deformity, current ear infection, and/or history of pulmonary or cardiac disease. Informed consent was obtained from study participants before they participated.

Data were collected into a secure data management system, RedCap (version 6.18.1, Vanderbilt University). Initial baseline vital signs (heart rate, blood pressure, respiratory rate, and oxygen saturation) were obtained and (heart rate, respiratory rate, and oxygen saturation) continually monitored throughout the study. End-tidal partial pressure of carbon dioxide ( $P_{ETCO_2}$ ) and percentage of fraction of inspired carbon dioxide ( $F_{ICO_2}$ ) were obtained at baseline and continuously monitored using an oral/nasal sample line with the Capnostream 20p monitor (Medtronic, Minneapolis, MN). The device measured the percentage of  $F_{ICO_2}$ , and it was used to calculate  $P_{CO_2}$ . A double limb circuit and 980 Puritan Bennett (Medtronic, Minneapolis, MN) ICU ventilator was used in this study. See Figure 1 for the study.

**FIGURE 1**  
Picture of the study setup.



**Study procedure**

We evaluated 4 NIV masks (two FFM and two ONM). The masks included BiTrac MaxShield with standard elbow (FFM) and BiTrac Full-Face with standard elbow (ONM) (Pulmodyne, Indianapolis, IN), Resprionics PerforMax with standard elbow (FFM), and Philips Resprionics AF531 with standard elbow (ONM) (Philips, Carlsbad, CA). The order of the masks applied to subjects were randomly chosen by paper raffling from a container.

All subjects performed 20 min on each mask followed by 5 min of a washout interval between masks. PEEP was set to 0, 2, 4, and 5 (5 min for each level), while pressure support remained at 5 cm H<sub>2</sub>O higher than PEEP.  $F_{ICO_2}$  and  $P_{ETCO_2}$  were collected at 4:00, 4:30, and 5:00 min mark for each PEEP setting. We averaged these three measurements.

Special precautions were followed. First, the study participants were required to refrain from eating at least 60 min before the study. The study would be stopped if subjects' heart rate changed by 20% from baseline for more than 1 min and/or complained of shortness of breath.

**Statistical analysis**

Descriptive statistics as means and standard deviations were calculated for initial heart rate, initial respiratory rate, initial oxygen saturation,  $F_{ICO_2}$ , and  $P_{ETCO_2}$ . For the dependent variable  $F_{ICO_2}$  median and interquartile ranges were determined. Comparison between  $F_{ICO_2}$  at all levels of PEEP and masks were not normally distributed so they were analyzed with Kruskal-Wallis test with  $p < 0.05$ . If significant differences were found from the Kruskal-Wallis tests, a post hoc analysis was performed using a Mann-Whitney  $U$  test to determine which PEEP levels significantly differed with  $p < 0.0083$  to control for family-wise error. These statistical tests were ran using SPSS version 22 premium (IBM, Chicago, Illinois).

**RESULTS**

Eight healthy participants consented to participate. Mean baseline data were heart rate of  $82 \pm 8$  beats/min, respiratory rate of  $16 \pm 3$  breaths/min, oxygen saturation of  $98\% \pm 1\%$ ,  $P_{ETCO_2}$  of  $37 \pm 3$  mmHg, and  $F_{ICO_2}$  of  $0.0 \pm 0.0\%$ .

The variables associated with each PEEP level are reported in Table 1. At a PEEP of 0, 2, 4, or 5 cm H<sub>2</sub>O there were no significant difference in the tidal volume or respiratory rate. Median  $F_{ICO_2}$  at 0 cm H<sub>2</sub>O PEEP was significantly higher compared to median  $F_{ICO_2}$  at 4 cm H<sub>2</sub>O PEEP ( $p = 0.001$ ) and 5 cm H<sub>2</sub>O PEEP ( $p < 0.001$ ). Median  $F_{ICO_2}$  at 2 cm H<sub>2</sub>O PEEP was significantly higher compared to median  $F_{ICO_2}$  at 5 cm H<sub>2</sub>O PEEP ( $p = 0.002$ ), see Figure 2. Median leak at 0 cm H<sub>2</sub>O PEEP was significantly lower compared to median leak at 2 cm H<sub>2</sub>O PEEP ( $p = 0.004$ ), 4 cm H<sub>2</sub>O PEEP ( $p < 0.001$ ), and 5 cm H<sub>2</sub>O PEEP ( $p < 0.001$ ). Median leak at 2 cm H<sub>2</sub>O PEEP was significantly lower compared to median leak at 5 cm H<sub>2</sub>O PEEP ( $p = 0.003$ ).

**TABLE 1**  
Measured variables at PEEP settings for all masks

PEEP setting	Median (IQR)			
	Leak, L/min	Tidal volume, mL	Respiratory rate, breaths/min	$F_{ICO_2}$ , %
PEEP 0 (n = 32)	22 (15–30) <sup>††</sup>	636 (503–892)	13 (12–17)	1.83 (0.66–4) <sup>§§</sup>
PEEP 2 (n = 32)	30 (25–40) <sup>†</sup>	646 (496–908)	15 (12–17)	1 (0.33–2.66) <sup>  </sup>
PEEP 4 (n = 32)	36 (27–41)	637 (498–938)	15 (12–18)	0.49 (0–1.92)
PEEP 5 (n = 32)	41 (33–47)	701 (481–968)	15 (13–18)	0 (0–0.92)

Note: PEEP = positive end-expiratory pressure, IQR = interquartile range.

\*Leak was significantly lower than at PEEP of 2 ( $p = 0.004$ ).

<sup>†</sup>Leak was significantly lower than at PEEP of 4 ( $p < 0.001$ ).

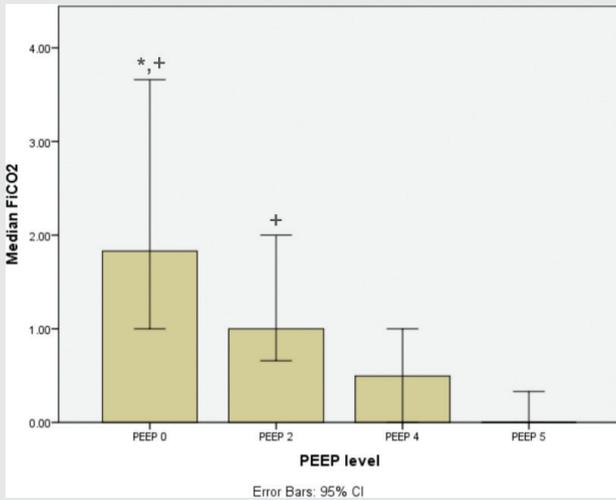
<sup>‡</sup>Leak was significantly lower than at PEEP of 5 ( $p < 0.001$ ;  $p = 0.003$ ).

<sup>§</sup> $F_{ICO_2}$  was significantly higher than at PEEP of 4 ( $p = 0.001$ ).

<sup>||</sup> $F_{ICO_2}$  was significantly higher than at PEEP of 5 ( $p < 0.000$ ;  $p = 0.003$ ).

**FIGURE 2**

Median fraction of inspired carbon dioxide ( $F_{iCO_2}$ ) at various positive end-expiratory pressure (PEEP) settings during NIV with full-face and oronasal masks.



\* $F_{iCO_2}$  was significantly higher than at PEEP of 4 ( $p = 0.001$ ).  
 + $F_{iCO_2}$  was significantly higher than at PEEP of 5 ( $p < 0.000$ ;  $p = 0.003$ ).

Median  $F_{iCO_2}$  with FFM Philips for all PEEP levels was significantly higher than median  $F_{iCO_2}$  of FFM Pulmodyne ( $p = 0.002$ ), ONM Pulmodyne ( $p < 0.001$ ), and ONM Philips ( $p = 0.002$ ). Individual  $F_{iCO_2}$  for each mask can be seen in Figure 3. Median leak with FFM Philips was significantly lower than median leak of FFM Pulmodyne ( $p = 0.001$ ). There were no significant differences in tidal volume and respiratory rate.

**DISCUSSION**

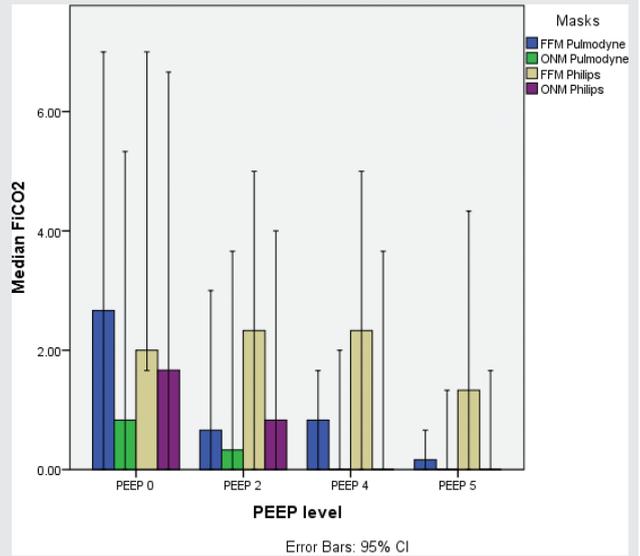
This study found that a PEEP of 5 cm H<sub>2</sub>O associated with the reported leak was required to washout CO<sub>2</sub> from the ONM and FFM when using a critical care ventilator with a dual limb circuit when data from the ONM and FFM were combined. This finding is illustrated in Figure 2. When examining each of the masks in Figure 3, PEEP of 4 cm H<sub>2</sub>O cleared most of the CO<sub>2</sub> when using ONM while at the PEEP of 5 cm H<sub>2</sub>O on the FFM some CO<sub>2</sub> still remained. This study is the first to assess CO<sub>2</sub> clearance from NIV masks while using a critical care ventilator and dual limb circuits. This study's findings impact in clinical settings are unknown, as the subjects were normal volunteers and had limited time on each PEEP level; however, a  $F_{iCO_2}$  of 1% to 4% would be equivalent to a partial pressure of CO<sub>2</sub> of 7.1–28.5 mmHg at sea level. This amount of rebreathing could elevate the arterial partial pressure of CO<sub>2</sub> [11]. Nevertheless, we didn't witness the impact of CO<sub>2</sub> rebreathing on the subjects' respiratory rate or work of breathing with  $F_{iCO_2}$  that was associated with the lowest PEEP level and leak level. This finding is likely due to the relatively short time spent at each PEEP level and the subsequent increase in PEEP levels.

Our reported findings with ONM are similar to what others have reported regarding clearing CO<sub>2</sub> from NIV masks while using a single limb circuit. Samolski et al. [7] reported that a PEEP or EPAP level as low as 4 cm H<sub>2</sub>O effectively washed out CO<sub>2</sub> while using a single limb circuit to provide NIV [7]. To the best of our knowledge, this study is the first to report similar findings on mask interfaces while using a dual limb circuit and critical care ventilator.

Holanda et al. [12], compared CO<sub>2</sub> washout on three types of NIV interfaces: nasal, oronasal, and total-face masks [12]. This study used a single limb circuit and CO<sub>2</sub> monitoring/sampling between the masks and expiratory

**FIGURE 3**

Median fraction of inspired carbon dioxide ( $F_{iCO_2}$ ) at various positive end-expiratory pressure (PEEP) settings during NIV with each full-face and oronasal masks. FFM Pulmodyne = Full-Face Mask Pulmodyne, ONM Pulmodyne = Oronasal Mask Pulmodyne, FFM Philips = Full-Face Mask Philips, ONM Philips = Oronasal Mask Philips.



port in the circuits. Their finding suggested that with total-face masks, CO<sub>2</sub> rebreathing is zero; however, the amount of mask leak was not reported and may have impacted CO<sub>2</sub> washout [12]. In our study, we measure  $F_{iCO_2}$  at the nose and mouth and found that as PEEP increased so did the leak measured by the ventilator while  $F_{iCO_2}$  decreased. Our finding suggests there may be a correlation between the degree of leak and CO<sub>2</sub> washout. Masks were fit on volunteers as recommended without overtightening, and volunteers did not perceive a leak nor did it impact ventilator synchrony. Others have reported that interface's dead space and amount of leakage impacts volume of inspired carbon dioxide ( $V_{iCO_2}$ ) [13]. In our study, the differences in dead space may have affect CO<sub>2</sub> rebreathing clearance as observed in Figure 3, since median  $F_{iCO_2}$  was higher for the full-face masks.

Our study has some limitations. The sample size was small, but the differences found were statically significant. These were also normal volunteers, and results may differ in someone who has an elevated  $P_{aCO_2}$  at baseline. Another limitation is the nasal cannula we used for  $F_{iCO_2}$  monitoring created a small leak. This leak could aid CO<sub>2</sub> removal. We also did not measure the impact of an elevated  $F_{iCO_2}$  on arterial  $P_{CO_2}$  or work of breathing. Additionally, we didn't measure the dead space of masks used in this study.

**CONCLUSION**

A PEEP of 5 cm H<sub>2</sub>O and its associated leak resulted in CO<sub>2</sub> washout most of the time in normal volunteers. As mask size increases, it requires a higher PEEP level resulting in a larger leak to washout CO<sub>2</sub>. Therefore, no or low PEEP levels that result in little to no leak should be avoided while using a critical care ventilator with a double limb circuit and ONM or FFM. These findings should be tested in patients with elevated arterial  $P_{CO_2}$  to determine the clinical impact of these findings.

**DISCLOSURES**

**Contributors**

All authors contributed to the conception or design of the work, the acquisition, analysis, interpretation of the data. All authors were involved

in drafting and commenting on the paper and have approved the final version. Specific contributions of each author: Mr. Al Hussain contributed literature search, data collection, study design, analysis of data, manuscript preparation and review. Dr. Vines contributed to study design, analysis of data, manuscript preparation and review.

#### Funding

Funded by the Department. No external funding.

#### Competing Interests

All authors have completed the ICJME uniform disclosure form at <http://www.icmje.org/disclosure-of-interest/> and declare: Mr. Al Hussain has no conflict of interest. Dr. Vines reports speaking for Theravance Biopharma and research funding from Teleflex Medical, Inc. and Rice Foundation.

#### Ethical Approval

Rush University's institutional review board approval was obtained and registered on Clinical trials.gov #: NCT03882723.

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