

Effects of flow on carbon dioxide washout and nasal airway pressure in healthy adult volunteers during the constant-flow mode in a non-invasive ventilator

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To the Editor: The essence of high-flow nasal cannula (HFNC) is a constant-flow mode in non-invasive ventilator (NIVCFM). The main mechanisms of NIVCFM/HFNC are dead-space washout and generation of low-level airway pressure, however, further evidence in adults is needed. Here, we measured the end-tidal carbon dioxide pressure (PetCO₂), end-expiratory pressure (EEP), and end-inspiratory pressure (EIP) at different depths of the nasal cavity during different flow rates of NIVCFM/HFNC to validate the respiratory physiological mechanisms of NIVCFM/HFNC in healthy adults: whether the carbon dioxide (CO₂) washing mechanism exists and its intensity, and how much EEP and EIP can be produced by NIVCFM/HFNC.

This study was approved by the Ethics Committee of Qilu Hospital of Shandong University (No. 2018213), and written informed consent was obtained from the participants.

Healthy adults were recruited if they were aged between 18 and 30 years. However, individuals with upper respiratory tract diseases, history of upper respiratory infection in the past 2 weeks, and history of smoking and who used drugs that influence cardiopulmonary function were excluded.

The subjects were placed in a vertical sitting position during the test and instructed to breathe with their mouth closed while wearing the HFNC (Veoflo[®], Flexicare Medical Ltd., Mountain Ash, UK). Conditioned room air (21% oxygen [O₂], 0.04% CO₂) was delivered by the NIVCFM/HFNC (GA ST40P, CURATIVE, Beijing, China) at flow rates of 0, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, and 60 L/min.

PetCO₂ was measured using the KMI605C device (Kingst History Data Review, Beijing, China). A CO₂ sampling tube (Jinglan Medical Equipment Limited Company, Suzhou, Jiangsu, China) was inserted into the nasal cavity at 2, 3, 4, and 5 cm. PetCO₂ data were recorded at real time and stored on a USB memory stick attached to the Kingst History Data Review version 2.0 (Kingst History Data Review). The average values of the maximum partial pressure of CO₂ in expired gas (ie, PetCO₂) during each breath within 3 min were calculated.

For the EEP and EIP measurements, a handheld digital RS232 manometer (AZ8252, AZ[®] Instrument Corp., Taiwan, China) was used. An anesthesia catheter (Henan Tuoren Medical Device Co., Ltd, Xinxiang, Henan, China) was inserted into the nasal cavity at 2, 3, 4, 5, and 6 cm. EEP and EIP data were continuously recorded and later analyzed on a personal computer using Handheld Meter's Data Logger version 3.10 (Kingst History Data Review). The mean EEP and EIP were calculated by averaging the pressure from the peak of expiration and inspiration of each breath during the 3-min recording.

PetCO₂, EEP, and EIP data were function-fitted using MATLAB 7.11 (MathWorks, Natick, MA, USA) Curve Fitting Toolbox. The data were analyzed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as counts and frequencies, and continuous variables as mean ± standard deviation when the data followed a normal distribution. At the same depth of nasal cavity, one-way analysis of variance (for data with normal distribution) followed by least significant difference (LSD) test or Kruskal-Wallis *H* test (for data with non-normal distribution) followed by Dunn's test was used to compare the PetCO₂, EEP, and EIP at different flow rates compared with 0 L/min. Statistical significance was established at a *P* value < 0.05.

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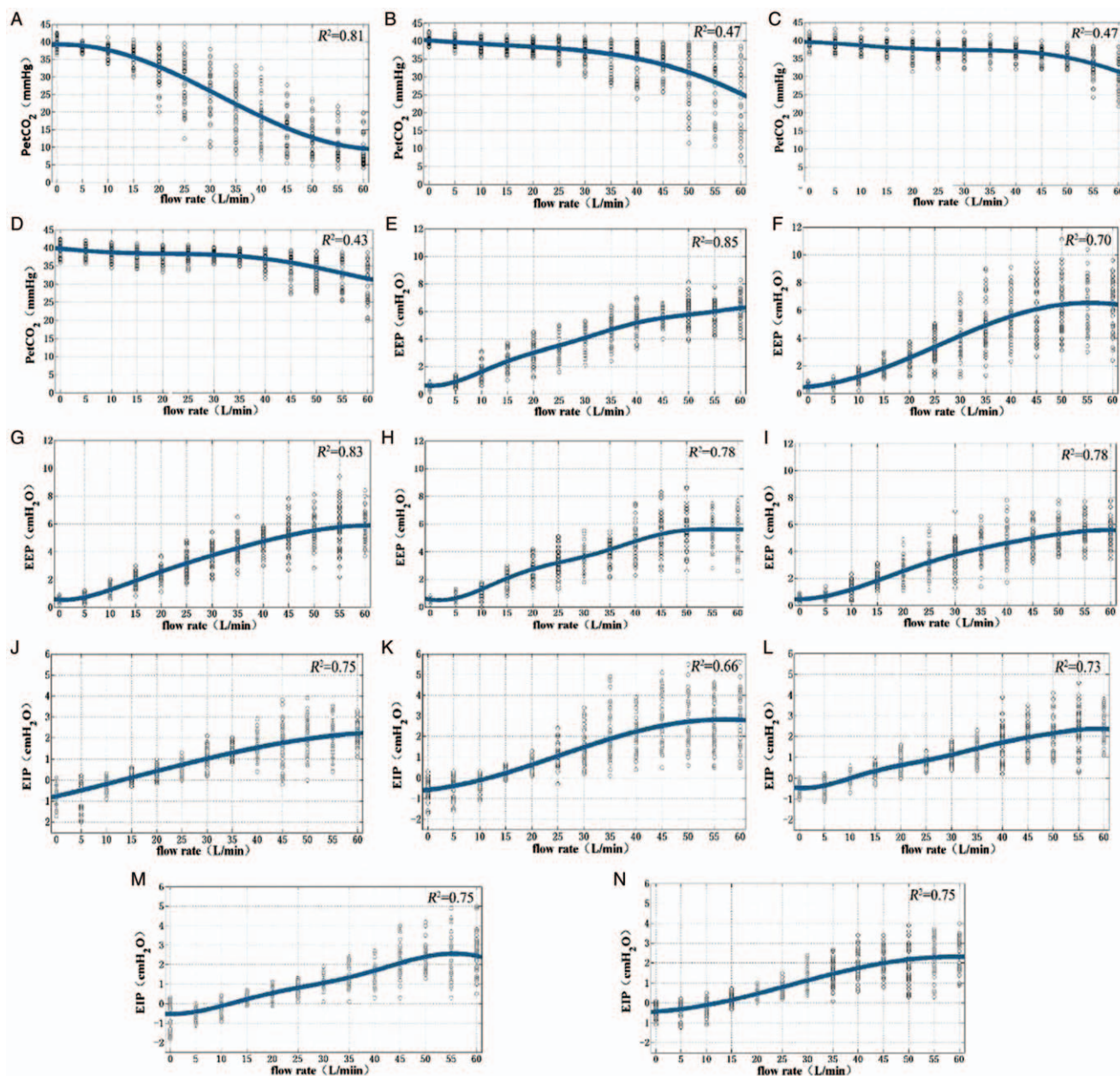


Figure 1: Fourier fitting curve of PetCO₂ at depths of 2 (A), 3 (B), 4 (C), and 5 cm (D) in the nasal cavity. Fourier fitting curve of EEP at depths of 2 (E), 3 (F), 4 (G), 5 (H), and 6 cm (I) in the nasal cavity and EIP at depths of 2 (J), 3 (K), 4 (L), 5 (M), and 6 cm (N) in the nasal cavity. EEP: End-expiratory pressure; EIP: End-inspiratory pressure; PetCO₂: End-tidal carbon dioxide pressure.

A total of 44 healthy adults participated in this study with a mean age of 23.1 ± 2.1 years and a body mass index of 21.9 ± 3.7 kg/m².

When the flow rate was 60 L/min, NIVCFM/HFNC reduced PetCO₂ by 30.2 mmHg from a baseline of 39.5 mmHg at a depth of 2 cm in the nasal cavity, but the PetCO₂ at 3, 4, and 5 cm depth in the nasal cavity decreased by only 14.9, 8.2, and 8.3 mmHg, respectively, compared with that at 0 L/min. The PetCO₂ was statistically different when the flow was ≥ 20 , ≥ 15 , ≥ 15 , and ≥ 30 L/min at a depth of 2, 3, 4, and 5 cm in the nasal cavity compared with that at 0 L/min (all $P < 0.05$). There is a strong non-linear negative correlation between PetCO₂

and flow rate ($R^2 = 0.81$) at a depth of 2 cm in the nasal cavity, but $R^2 < 0.50$ at a depth of 3, 4, and 5 cm of the nasal cavity [Figure 1A–1D].

At 60 L/min and the depth of 3 cm, the mean EEP during the 3-min recording reached 6.5 cmH₂O. EEP was statistically different at different depths in the nasal cavity when the flow rate was ≥ 15 L/min compared with that at 0 L/min (all $P < 0.05$). There was a strong non-linear positive correlation between the EEP and flow rate ($R^2 > 0.70$) at a depth of 2, 3, 4, 5, and 6 cm in the nasal airway. NIVCFM/HFNC induced a significant increase in EEP after 3 min of respiratory support, while the curves became stable when the flow rate was >45 L/min [Figure 1E–1I].

At 60 L/min and the depth of 3 cm, EIP reached 2.9 cmH₂O. EIP was statistically different at different depths of the nasal cavity when the flow was ≥ 20 L/min compared with that at 0 L/min (all $P < 0.05$). There is a strong non-linear positive correlation between the EIP and flow rate ($R^2 > 0.66$) at a depth of 2, 3, 4, 5, and 6 cm in the nasal cavity. As the flow rate increased, EIP demonstrated a small but significant increase after 3 min of respiratory support, while the curves became stable when the flow rate was > 50 L/min [Figure 1J–1N].

The results of this study showed that NIVCFM/HFNC has an extremely limited washing effect on end-expiratory CO₂ beyond nasal limen in healthy adults, and as the depth increases, the flushing effect on end-expiratory CO₂ decreases rapidly. The greater the depth, the higher the flow required to wash out the CO₂ in expired gas. Ritchie *et al*^[1] used HFNC in ten healthy adults and found that the end-expiratory CO₂ concentration at the oropharynx did not change with the increase in flow. Other scholars have also obtained the same results.^[2,3] The reasons may be as follows: (1) Complexity of the anatomical structure of the upper airway leads to difficulty of the NIVCFM/HFNC gas to enter deeper locations. (2) Mündel *et al*^[4] considered that the main reason for the improvement of respiratory efficiency after using NIVCFM/HFNC is that the increase in flow rate leads to deep and slow breathing, which in turn results in an increase in tidal volume rather than a decrease in anatomical dead space.

This study found that, when the flow rate of the NIVCFM/HFNC was greater than the adult's peak inspiratory flow rate, only low-level EEP and EIP could be produced with the mouth closed. In patients with peak inspiratory flow > 60 L/min and who cannot breathe with the mouth closed, NIVCFM/HFNC provides extremely limited positive pressure assistance and should be used with caution. There is a non-linear positive correlation between the EEP and EIP in the nasal cavity and flow rate, which is consistent with Kumar's study.^[5] However, when the flow rate is > 45 or > 50 L/min, there is no significant increase in EEP and EIP with the increase in flow rate. This may be because the upper airway muscles, especially the nasal ala muscles, have a certain tension and, as the flow increases, the muscles become increasingly stiff, leading to greater expiratory resistance.^[4] However, the upper airway muscle tension is limited. Therefore, after the flow rate reaches a certain value, the

airway pressure does not significantly change with the flow rate.

The conclusions of this study are as follows: the NIVCFM/HFNC has an extremely limited washing effect on CO₂ in expired gas beyond nasal limen in healthy adults, and as the depth increases, the flushing effect on CO₂ in expired gas decreases rapidly; the NIVCFM/HFNC can only produce low-level EEP (≤ 6.5 cmH₂O) and EIP (≤ 2.9 cmH₂O) in the nasal cavity of healthy adults when breathing with the mouth closed.

Declaration of patient consent

The authors certify that they have obtained all appropriate consent forms from study subjects. In the form, the study subject(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The study subjects understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

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