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### A flow-leak correction algorithm for pneumotachographic work-of-breathing measurement during high-flow nasal cannula oxygen therapy

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#### ABSTRACT

Measuring work of breathing (WOB) is an intricate task during high-flow nasal cannula (HFNC) therapy because the continuous unidirectional flow toward the patient makes pneumotachography technically difficult to use. We implemented a new method for measuring WOB based on a differential pneumotachography (DP) system, equipped with one pneumotachograph inserted in the HFNC circuit and another connected to a monitoring facemask, combined with a leak correction algorithm (LCA) that corrects flow measurement errors arising from leakage around the monitoring facemask. To test this system, we used a mechanical lung model that provided data to compare LCA-corrected respiratory flow, volume and time values with effective values obtained with a third pneumotachograph used instead of the LCA to measure mask flow leaks directly. Effective and corrected volume and time data showed high agreement (Bland– Altman plots) even at the highest leak. Studies on two healthy adult volunteers confirmed that corrected respiratory flow combined with esophageal pressure measurements can accurately determine WOB (relative error < 1%). We conclude that during HFNC therapy, a DP system combined with a facemask and an algorithm that corrects errors due to flow leakages allows pneumotachography to measure reliably the respiratory flow and volume data needed for calculating WOB.

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#### 1. Introduction

High-flow oxygen therapy through a nasal cannula (HFNC) is increasingly used as a technique for treating respiratory failure [1]. Delivery of a heated and humidified oxygen/air mixture at high

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flow rates improves ventilatory efficiency and generates a positive pharyngeal pressure that reduces the work of breathing (WOB) [2]. In current practice, HFNC therapy is initiated at a flow rate of 1 L/kg/min + 1 and flow is then titrated according to respiratory distress [3]. Whether this procedure does so safely nevertheless remains uncertain, because subsequent variations in flow settings fail to take into account effective changes in a patient's WOB.

WOB is the reference standard variable for measuring respiratory muscle workload [4] and is mathematically expressed as WOB =  $\int$  Pressure  $\times$  Volume. Yet, WOB might indicate the actual effort necessary for the patient to breathe inaccurately, because it fails to consider the energy expended during the isometric phase of respiration. The pressure time product (PTP) is a variable that directly measures the respiratory effort during the dynamic and isometric respiratory phases [5]. Despite extensive physiologic evidence supporting the use of WOB and PTP for establishing whether the various ventilation modalities effectively unload respiratory muscles [6], less conclusive evidence supports monitoring WOB and PTP in clinical practice. In recent years, Milesi et al., in their recommendations for daily use of HFNC in pediatrics, mention esophageal pressure ( $P_{eso}$ ) measurement as a useful mode to

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Abbreviations: ANOVA, analysis of variance; CPAP, continuous positive airway pressure; CV, coefficient of variation; DP, differential pneumotachography; e\_iWOBtot, effective iWOBtot; e\_iPTPtot, effective iPTPtot; e\_Te, effective Te; e\_Ti, effective Ti; e\_Vte, effective Vte; e\_Vti, effective Vti; fc, flow-corrected; F-LCA, flow-LCA; HFNC, high-flow nasal cannula; iPTPtot, inspiratory total PTP; iWOBtot, inspiratory total WOB; LCA, leak correction algorithm; mfl, mean flow line; Patm, atmospheric pressure; pc, pressure-corrected; PEEP, positive end expiratory pressure; Peso, esophageal pressure; P-LCA, pressure-LCA; PMask, pressure inside the facemask; PNT, pneumotachograph; PTP, pressure time product; iPTP<sub>tot</sub>, inspiratory total pressure time product; RE, relative error; R<sub>Mask\_Leak</sub>, mask leak channel resistance; R<sub>Mask\_PNT-B</sub>, mask PNT-B resistance; RR, respiratory rate; SD, standard deviation; Te, expiratory time; Ti, inspiratory time; V<sub>HFNC\_PNT-A</sub>, HFNC flow via PNT-A; V<sub>Mask\_Leak</sub>, flow leakage from the facemask rim;  $V_{Mask\_Leak\_PNT-C}$ , facemask flow leakage via PNT-C;  $\dot{V}_{Mask\_PNT-B}$ , facemask flow via PNT-B;  $\dot{V}_{Resp}$ , respiratory flow; Vt, tidal volume; Vte, expiratory tidal volume; Vti, inspiratory tidal volume; zfl, zero flow line; WOB, work of breathing.

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**Fig. 1.** Configuration of a differential pneumotachography system during high-flow nasal cannula therapy. Respiratory flow measurement during high-flow nasal cannula (HFNC) therapy using a differential pneumotachography (DP) system with one pneumotachograph (PNT) inserted in the HFNC circuit (PNT-A), and another (PNT-B) applied to a monitoring mask placed on an infant's face to cover the nose and the mouth.

quantify the inspiratory effort in infants with bronchiolitis requiring HFNC therapy [3]. They also suggest that calculating PTP on  $P_{eso}$ measurements in these patients with high intrinsic positive end expiratory pressure (PEEP) may help to adjust external PEEP and reduce the inspiratory effort [7]. Although many physicians caring for critically ill patients recognize the clinical importance of monitoring WOB during HFNC, they neglect to use  $P_{eso}$  or its derivate variables (i.e., WOB and PTP) because this approach raises technical difficulties.

In spontaneously breathing patients, the traditional way to assess WOB and PTP entails simultaneously acquiring Peso and respiratory flow  $(\dot{V}_{Resp})$  signals. In HFNC-assisted patients, an accurate  $\dot{V}_{Resp}$  signal is difficult to obtain. A previous study from our group showed that a reliable way to estimate  $\dot{V}_{Resp}$  during HFNC is to measure the flow difference detected by two pneumotachographs (PNTs) [8,9], one inserted in the HFNC breathing circuit, and another applied to a monitoring facemask placed on the patient's face to cover the nose and the mouth without leaving gaps [10] (Fig. 1). Although we were especially careful to apply the monitoring facemask tight on the infants' face and on some occasions used a soft sealing material to improve adhesion, obtaining a tight seal was not always feasible, especially in uncooperative young children, who often needed light sedation to accept the facemask. Even moderate leaks shifted the mean differential flow upwards and caused a drift in tidal volume (Vt), thus affecting  $\dot{V}_{Resp}$  and volume calculations (Fig. 2). Hence, a possible solution to avoid pressing the mask on the patient's face is an algorithm that measures and corrects the flow leaks around the monitoring facemask.

In this bench study, we used a mechanical lung model simulating assisted breathing through an HFNC system to test whether a differential pneumotachography (DP) system, including a PNT placed in the HFNC circuit and another connected to the airways via a facemask, when combined with an algorithm that corrects the errors due to the flow leaks from the monitoring facemask (leak correction algorithm, LCA), can accurately measure volume and time data. *In vivo*, we verified whether the DP system combined with the LCA yielded the corrected  $\dot{V}_{Resp}$  and volume data needed to calculate the inspiratory total WOB (iWOB<sub>tot</sub>) and inspiratory total PTP<sub>tot</sub> (iPTP<sub>tot</sub>).

### 2. Methods

#### 2.1. Subjects

Two healthy adult subjects volunteered for WOB and PTP measurements. Both received HFNC (Fisher and Paykel Healthcare, Irvine, CA, USA) therapy at an airflow rate of 20 L/min. A PNT (PNT-A) (3700 series, non-heated, 0-160 LPM; Hans Rudolph, Kansas City, MO, USA) combined with a differential pressure transducer (SensorTechnics 144LU01D-PCB, Sensortechnics, Inc., Mansfield, CA, USA) was inserted in series with the HFNC breathing circuit to measure HFNC flow ( $V_{HFNC PNT-A}$ ).  $P_{eso}$  as a surrogate for pleural pressure was measured with a single solid-state catheter-tip pressure transducer (CTO-1, Gaeltec, Dunvegan, Scotland). Proper catheter placement into the lower third of the esophagus was confirmed using the occlusion technique [11]. A monitoring facemask equipped with a second PNT (PNT-B) was placed on the subject's face to cover the nasal cannula and the mouth (Fig. 1), to detect flow crossing the mask through the PNT-B ( $\dot{V}_{Mask PNT-B}$ ). The monitoring facemask was sealed on the subject's face using Rapid Soft Putty (Coltene, Switzerland). A plastic tube was connected to an inlet on the monitoring facemask to simulate a Vt leak of 70% (a condition corresponding to the monitoring facemask comfortably placed on the subject's face). A third PNT (PNT-C) was inserted in series between the monitoring facemask and the leak tube to measure effective flow leak signal ( $\dot{V}_{Mask\_Leak\_PNT-C}$ ) and thus effective  $\dot{V}_{Resp}$ . To detect pressure inside the mask ( $P_{Mask}$ ), a small tube was used to connect the monitoring facemask to a differential pressure transducer (SensorTechnics 144LU10D-PCB, Sensortechnics, Inc., Mansfield, CA, USA). Once the sensors were calibrated and equalized, the volunteer started to breathe at a respiratory rate (RR) of 20 breaths/min to simulate labored breathing.  $P_{eso}$ ,  $P_{Mask}$  and the flow signals detected by the three PNTs were simultaneously recorded and their data used for calculating effective and corrected iWOBtot and iPTPtot. Statistical data were obtained from 15 consecutive breaths for each subject.

#### 2.2. Mechanical lung model

Bench studies took place in the Pediatric Critical Care Pulmonary Laboratory, Department of Pediatrics, Sapienza University of Rome. To simulate an infant breathing, we used a custommade mechanical lung model, including a high precision motordriven 60 mL-syringe, generating sinusoidal flow waveforms with adjustable RR and Vt (Fig. 3). The syringe adapter was connected to a double Y, with one side simulating the upper airway connected with the HFNC and its PNT (PNT-A) (8311 series, nonheated, 0-10 LPM; Hans Rudolph, Kansas City, MO, USA) combined with a pressure transducer (SensorTechnics 144LU01D-PCB, Sensortechnics, Inc., Mansfield, CA, USA), another side simulating the monitoring facemask equipped with a PNT (PNT-B), and the third side connected through a PNT (PNT-C) to tubes of increasing length that simulated different flow leaks. A small tube connected the double Y with a differential pressure transducer (SensorTechnics 144LU10D-PCB, Sensortechnics, Inc., Mansfield, CA, USA) to detect the pressure inside the simulating monitoring facemask ( $P_{Mask}$ ). In this study, because Vt is commonly used to monitor air tightness during invasive and noninvasive ventilation in children [12], we defined the degree of mask leakage as follows: Vt leak (%) = 100  $\frac{\text{(inspiratory Vt} - expiratory Vt)}{\text{inspiratory Vt}}$ .

We tested our system with six Vt leak percentages (0, 13, 32, 55, 74, and 86%). All variables were measured by setting the lung simulator with a flow rate of 5 L/min, a Vt of 30 mL, inspiratory time (Ti) and expiratory time (Te) of 0.50 s and RR of 60 rpm, adapted to the values in spontaneously breathing infants. Because pneumotachographic measurements may be affected, albeit to

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