F_{IO_2} in an Adult Model Simulating High-Flow Nasal Cannula Therapy

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BACKGROUND: High-flow nasal cannula therapy (HFNC) is widely used for patients with acute respiratory failure. HFNC has a number of physiological effects. Although F_{IO_2} is considered to be constant, because HFNC is an open system, F_{IO_2} varies according to inspiratory flow, tidal volume (V_T), and HFNC gas flow. We investigated the influence of HFNC gas flow and other respiratory parameters on F_{IO_2} during HFNC. METHODS: We evaluated an HFNC system and, for comparison, a conventional oxygen therapy system. The HFNC apparatus was composed of an air/oxygen blender, a heated humidifier, an inspiratory limb, and small, medium, and large nasal prongs. HFNC gas flow was set at 20, 40, and 60 L/min, and F_{IO_2} was set at 0.3, 0.5, and 0.7. We measured F_{IO_2} for 1-min intervals using an oxygen analyzer and extracted data for the final 3 breaths of each interval. Spontaneous breathing was simulated using a mechanical ventilator connected to the muscle compartment of a model lung. The lung compartment passively moved with the muscle compartment, thus inspiring ambient air via a ventilator limb. With a decelerating flow waveform, simulated V_T was set at 300, 500, and 700 mL, breathing frequency at 10 and 20 breaths/min, and inspiratory time at 1.0 s. RESULTS: With HFNC gas flow of 20 and 40 L/min, at all set F_{IO_2} values, inspiratory oxygen concentration varied with V_T ($P < .001$). As the set value for F_{IO_2} increased, the difference between set F_{IO_2} and measured F_{IO_2} increased. Neither breathing frequency nor prong size influenced F_{IO_2}. CONCLUSIONS: During HFNC with simulated spontaneous breathing, when HFNC gas flow was 60 L/min, measured F_{IO_2} was similar to set F_{IO_2} at 0.3 and 0.5, whereas at 0.7, as V_T increased, measured F_{IO_2} decreased slightly. However, at 20 or 40 L/min, changes in V_T related with deviation from set F_{IO_2}. *Key words: spontaneous breathing; oxygen therapy; gas blender; oxygen analyzer; gas flow; nasal prong.* [Respir Care 2017;62(2):193–198. © 2017 Daedalus Enterprises]

Introduction

Oxygen therapy is the first-line treatment for patients with organ dysfunction.[1] For therapy, nasal cannulas and face masks are popular means of low-flow oxygen delivery. Via nasal cannula, oxygen flow is usually 1–6 L/min, and with an oxygen mask, a maximum flow of 15 L/min can be obtained. Meanwhile, inspiratory flow of patients with acute hypoxemic respiratory failure varies from 30 to >120 L/min,[2] and actual F_{IO_2} depends on the patient's breathing pattern; consequently, F_{IO_2} is usually lower than assumed.[3]

High-flow nasal cannula (HFNC) therapy has come into widespread use for patients with respiratory failure.[4,5] An air/oxygen blender generates a flow of up to 60 L/min, and the gas is heated and humidified with an active humidifier and subsequently delivered through a limb with a heating wire and via wide-bore nasal prongs. The F_{IO_2} of respiratory gas can be adjusted to between 0.21 and 1.0. Adequately heated and humidified high-flow gas delivers some physiological benefits as well as improving thoraco-abdominal synchrony[6] and washout of carbon dioxide in nasopharyngeal dead space.[7] High flow creates positive end-expiratory nasopharyngeal pressure[8,9,10] and is more

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The authors have disclosed no conflicts of interest.

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comfortable than other noninvasive ventilation and air-entrainment masks.[10,11] Physicians can also have greater confidence in the actual F_{IO_2} being delivered to the patient.[12] F_{IO_2} depends, however, on the relationship between patient inspiratory flow and HFNC gas flow.[13] We carried out this bench study to evaluate F_{IO_2} during HFNC with various spontaneous breathing patterns and with different prong sizes.

QUICK LOOK

Current knowledge

HFNC can deliver, via wide-bore nasal prongs, up to 60 L/min of heated and humidified medical gas to a patient. Beneficial effects of HFNC include warming and humidification of inspiratory gas, a great advantage over other modes of oxygen delivery; reduction of thoraco-abdominal asynchrony; washout of carbon dioxide in nasopharyngeal dead space; low levels of PEEP; and a reliable supply of F_{IO_2}.

What this paper contributes to our knowledge

With HFNC gas flow of 20 and 40 L/min, as V_T increased, measured F_{IO_2} was less than set F_{IO_2}. When HFNC gas flow was 60 L/min, measured F_{IO_2} was similar to set F_{IO_2}. As set F_{IO_2} increased, the difference between set F_{IO_2} and measured F_{IO_2} increased.

Methods

Experimental Apparatus

We compared 2 delivery systems: HFNC (Optiflow, Fisher & Paykel Healthcare, Auckland, New Zealand) and conventional nasal cannula (Hudson RCI Softech, Teleflex Japan, Tokyo, Japan). The HFNC incorporates an air/oxygen blender with flow meter (OA2060, San-You Technology, Saitama, Japan) and a heated humidifier (MR850, Fisher & Paykel Healthcare, Auckland, New Zealand). HFNC gas flow was set at 20, 40, and 60 L/min, and F_{IO_2} was set at 0.3, 0.5 and 0.7. A conventional nasal cannula was directly connected to a flow meter (P311, 1–15 L/min, Gunma Koike, Gunma, Japan), and flow was set at 2, 4, and 6 L/min at $F_{IO_2} = 1.0$. Flow from the flow meter of HFNC was measured with a pneumotachometer (4700 series, 0–160 L/min, Hans Rudolph, Inc, Shawnee, Kansas) connected to a differential pressure transducer (TP-602T, ±5 cm H_2O, Nihon Kohden, Tokyo, Japan). F_{IO_2} of HFNC gas was also confirmed by an oxygen analyzer (LZ100, San-You Technology).

To simulate adult external nares, we opened 2 holes in a polyvinyl chloride cylinder (internal diameter 8 mm, length 10 mm, external naris area 83 mm^2). One side of the cylinder was closed, and the nasal prongs were inserted into these holes (Fig. 1). The external nares were connected to a TTL test lung (TTL model 1601, Michigan Instruments, Grand Rapids, Michigan) via a standard ventilator circuit (22-mm Smoothbore system, 1.6 m, Intersurgical, Berkshire, United Kingdom). HFNC nasal prongs of 3 sizes, small, medium, and large (OPT542, OPT544, and OPT546, Fisher & Paykel Healthcare), and a conventional Softech nasal cannula were tested. Ratio of the cannula area to the area of external naris was 0.4 with large, 0.28 with medium, 0.15 with small, and 0.17 with conventional nasal cannula.

Simulated Spontaneous Breathing

Spontaneous breathing was simulated using a mechanical ventilator (Puritan-Bennett 840, Covidien, Carlsbad, California) and the TTL test lung. The muscle and lung compartments of the test lung were connected. The Puritan-Bennett 840 inflated the muscle compartment, causing the lung compartment to passively inflate, thus inspiring, along with ambient air, medical gas delivered via the HFNC or conventional nasal cannula being tested. The ventilator was set in volume control with descending ramp flow waveform. One-way valves prevented mixing of inspired and expired gases. Compliance of the TTL test lung was 0.05 L/cm H_2O, and resistance was 5 cm H_2O/L/s. Protocols were carried out with tidal volumes (V_T) of 300, 500, and 700 mL and breathing frequencies 10 and 20 breaths/min. Inspiratory time was set at 1 s with decelerating flow waveform, and it resulted in 33, 55, and 77 L/min of spontaneous breathing inspiratory peak flow.

Experimental Settings

Before experimental testing, a ventilator self-test was performed. HFNC creates PEEP and increases residual volume in the lung compartment. We measured the end-expiratory pressure of the lung compartment and kept the residual volume of the muscle compartment at the same level as the lung compartment by setting corresponding levels of PEEP on the Puritan-Bennett 840. Flow to the lung compartment was measured with a pneumotachometer (4700 series, 0–160 L/min, Hans Rudolph, Inc) connected to a differential pressure transducer (TP-602T, ±5 cm H_2O), and V_T was calculated by digital integration. The heated humidifier was turned off during these protocols. After each experimental setting was changed, we allowed ≥5 min for stabilization. The F_{IO_2} of inspired gas downstream of the external nares was measured for 1 min using an oxygen analyzer (LZ100), and data for the final 3 breaths were extracted. The oxygen

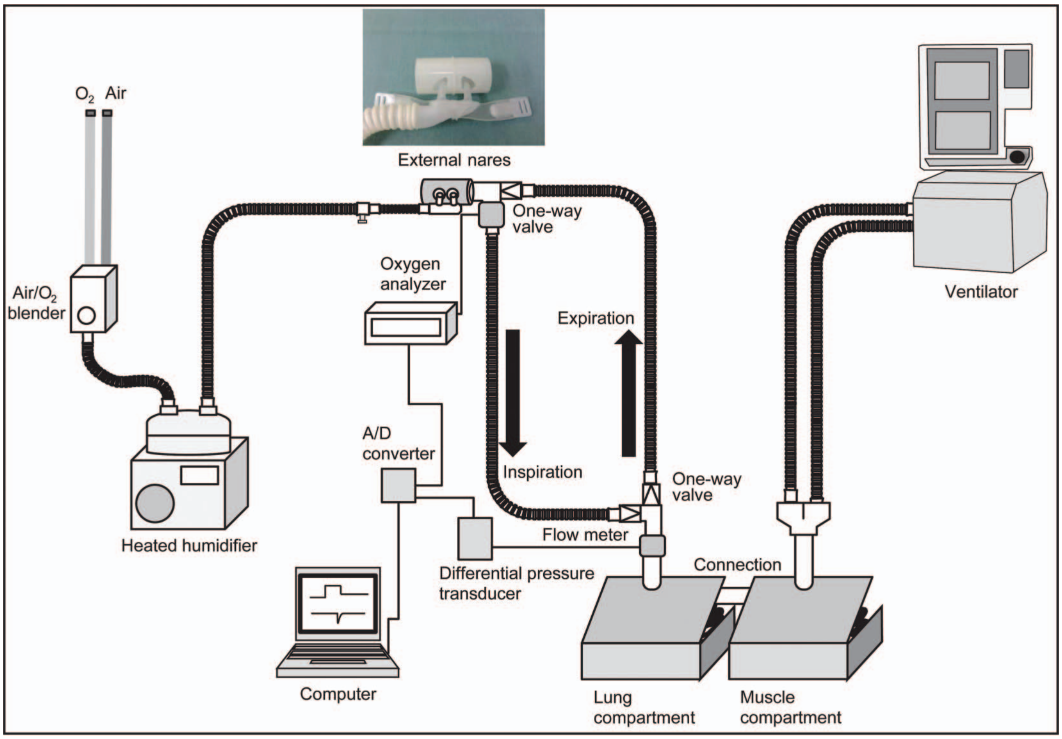

Fig. 1. The high flow nasal cannula (HFNC) system incorporated an air/O_2 blender with a flow meter and a heated humidifier. For the HFNC protocols, nasal prongs were connected to the manufacturer's standard circuit. We made 2 holes in a polyvinyl chloride cylinder to simulate adult external nares. The external nares were connected to the TTL test lung via a standard ventilator circuit. Spontaneous breathing was simulated using a mechanical ventilator and TTL test lung. To simulate spontaneous breathing, the muscle and lung compartment of the test lung were connected; consequently, the mechanical ventilator inflated the muscle compartment, whereupon the lung compartment inspired, along with ambient air, medical gas delivered, in turn, via each of the HFNC prongs and a conventional low-flow cannula. To monitor V_T delivered to the lung compartment, flow to the lung compartment was measured using a pneumotachometer with a differential pressure transducer. Inspired gas downstream of the external nares was measured using an oxygen analyzer.

analyzer was calibrated at F_{IO_2} of 0.21 and 1.0. The pneumotachometer was calibrated with a supersyringe. All signals were processed through an analog/digital converter and saved on a computer at 50 Hz/channel using data acquisition software (WinDaq, Dataq Instruments, Akron, Ohio).

Statistics

At each experimental setting, we gathered F_{IO_2} data for 3 breaths. Analysis of variance was performed using repeated measures, and results are expressed as mean ± SD. All statistical tests were 2-sided, and $P < .01$ was considered statistically significant. All statistical analysis was performed using commercial software (SPSS 11.01, SPSS, Chicago, Illinois).

Results

With the HFNC system, when F_{IO_2} was set at 0.3, 0.5, and 0.7, oxygen concentration at the flow meter outlet was 0.31 ± 0.01, 0.51 ± 0.01, and 0.71 ± 0.01. With the conventional nasal cannula, when F_{IO_2} was set at 1.0, oxygen concentration was 1.00 ± 0.001. With HFNC, when gas flow was set at 20, 40, and 60 L/min, measured flow was 20.5 ± 0.3, 40.6 ± 0.7, and 58.8 ± 0.2 L/min; with the conventional nasal cannula, when gas flow was set at 2, 4, and 6 L/min, measured flow was 2.1 ± 0.3, 4.1 ± 0.2, and 6.2 ± 0.1 L/min. At HFNC gas flow of 20, 40, and 60 L/min, end-expiratory pressure of the lung compartment was 1.3 ± 0.3, 1.8 ± 0.3, and 2.2 ± 0.3 cm H_2O with the small prong; 1.7 ± 0.4, 2.8 ± 0.5, and 4.8 ± 0.5 cm H_2O with the medium prong; and 2.3 ± 0.6, 5.3 ± 0.6, and 10.3 ± 1.3 cm H_2O with the large prong.

As the set F_{IO_2} increased, the difference between set and measured F_{IO_2} increased ($P < .001$). The differences were 0.001 ± 0.017, 0.040 ± 0.048, and 0.073 ± 0.081 at set F_{IO_2} of 0.3, 0.5, and 0.7.

Effect of V_T and Gas Flow During HFNC

At HFNC, gas flows of 20 and 40 L/min, as V_T increased, measured F_{IO_2} decreased from set value ($P < .001$). At 60 L/min, whereas measured F_{IO_2} was not affected by

V_T when F_{IO_2} was set at 0.3 and 0.5, when F_{IO_2} was set at 0.7, as V_T increased, measured F_{IO_2} decreased from set value ($P = .001$) (Table 1) (Fig. 2).

Effect of V_T and Gas Flow During Conventional Nasal Cannula Delivery

As V_T increased, measured F_{IO_2} statistically significantly decreased at all gas flows ($P < .001$) (Fig. 3). Measured F_{IO_2} during low-flow delivery with V_T of 300, 500, and 700 mL was 0.37 ± 0.01, 0.32 ± 0 and 0.29 ± 0 at 2 L/min; 0.45 ± 0.01, 0.39 ± 0.01, and 0.34 ± 0 at 4 L/min; and 0.58 ± 0.01, 0.45 ± 0.01, and 0.40 ± 0 at 6 L/min.

Table 1. Effect of Tidal Volume and High-Flow Nasal Cannula Gas Flow on F_{IO_2}

Set F_{IO_2}	Flow (L/min)	V_T (mL)		
		300	500	700
0.3	20	0.29 ± 0	0.27 ± 0.01	0.26 ± 0.01
	40	0.30 ± 0	0.30 ± 0	0.29 ± 0.01
	60	0.31 ± 0	0.31 ± 0	0.31 ± 0
0.5	20	0.46 ± 0.02	0.40 ± 0.03	0.36 ± 0.02
	40	0.49 ± 0.02	0.48 ± 0.01	0.45 ± 0.02
	60	0.50 ± 0	0.50 ± 0	0.50 ± 0
0.7	20	0.62 ± 0.02	0.53 ± 0.04	0.46 ± 0.03
	40	0.69 ± 0	0.66 ± 0.01	0.61 ± 0.04
	60	0.70 ± 0	0.69 ± 0.01	0.69 ± 0.01

Effect of Breathing Frequency

We found no effect of breathing frequency on measured F_{IO_2}. Measured F_{IO_2} values at breathing frequencies of 10 and 20 breaths/min during HFNC were: at set $F_{IO_2} = 0.3$, 0.29 ± 0.02 and 0.29 ± 0.02; at set $F_{IO_2} = 0.5$, 0.46 ± 0.05 and 0.46 ± 0.05; and at set $F_{IO_2} = 0.7$, 0.63 ± 0.08 and 0.63 ± 0.08. Measured F_{IO_2} with the conventional nasal cannula at 10 and 20 breaths/min was 0.40 ± 0.08 and 0.40 ± 0.09.

Effect of Prong Size During HFNC

When we tested different prong sizes, we found no differences in measured F_{IO_2}.

Discussion

In this bench study, we evaluated how HFNC flow, V_T, breathing frequencies, and prong sizes affected measured F_{IO_2} during simulated spontaneous breathing. When HFNC gas flow was <40 L/min, measured F_{IO_2} was affected by V_T. As the F_{IO_2} set value was increased, the difference between the set value and measured F_{IO_2} increased. As HFNC gas flow increased, measured F_{IO_2} increased more toward the set value.

As a working hypothesis, if we assume that when HFNC gas flow is set at 20, 40, and 60 L/min, if all of the HFNC gas flow is inhaled, then measured F_{IO_2} would depend on the relationship between the V_T of spontaneous breathing

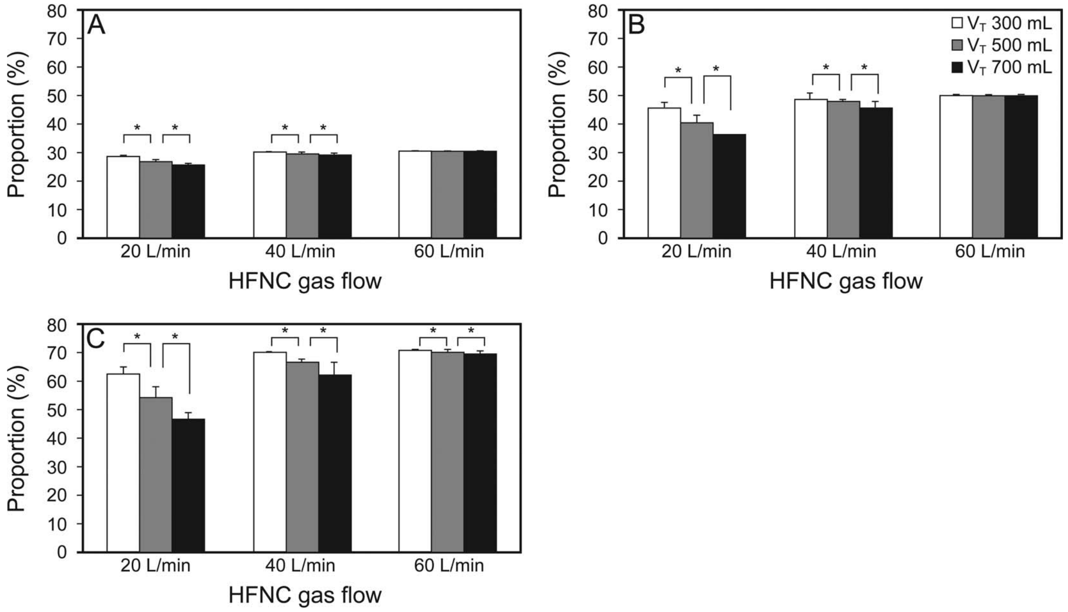

Fig. 2. Effect of changing V_T and flow during high-flow nasal cannula (HFNC) with F_{IO_2} of 0.3 (A), 0.5 (B), and 0.7 (C). With HFNC flows of 20 and 40 L/min, measured F_{IO_2} was affected by V_T at all F_{IO_2} settings. With HFNC flow of 60 L/min, measured F_{IO_2} was not affected by V_T when F_{IO_2} was set at 0.3 and 0.5; when F_{IO_2} was set at 0.7, however, as V_T increased, measured F_{IO_2} decreased. *, $P < .01$.

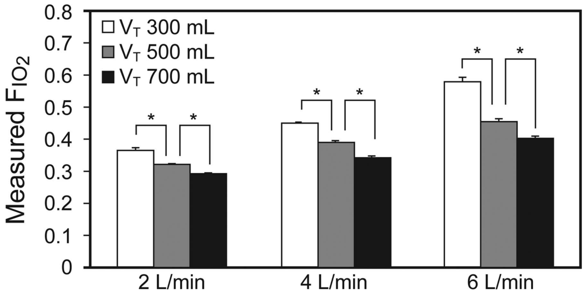

Fig. 3. Effects of changing V_T and flow during low-flow oxygen delivery As V_T increased, measured F_{IO_2} decreased significantly at all flow settings. *, $P < .001$.

and HFNC gas flow. When inspiratory flow is less than HFNC gas flow, the patient would, in theory, inhale the gas delivered via HFNC, and measured F_{IO_2} would consequently show good correspondence with set F_{IO_2}. If inspiratory flow were greater than HFNC flow, however, both delivered gas and ambient air would be inhaled. Chanques et al[10] previously reported that actual F_{IO_2} of the trachea in subjects with high-flow oxygen therapy increased as HFNC flow increased. When V_T was set at 300, 500, and 700 mL and inspiratory time was set at 1 s with a decelerating flow waveform, spontaneous breathing inspiratory peak flow was 33, 55, and 77 L/min. At V_T = 300 mL, for one third of the inspiratory time, spontaneous breathing inspiratory flow was >20 L/min. When V_T was 500 mL, for one fourth of the inspiratory time, spontaneous breathing inspiratory flow was >40 L/min. Consequently, with HFNC gas flow of 20 and 40 L/min, measured F_{IO_2} was affected by V_T. The difference between set F_{IO_2} and measured F_{IO_2} (ΔF_{IO_2}) was more apparent when set F_{IO_2} was high because the difference between the set F_{IO_2} and the F_{IO_2} of air (0.21) was greater. At V_T = 700 mL, when HFNC gas flow was 20 L/min, ΔF_{IO_2} was 0.04, 0.14, and 0.24 at set F_{IO_2} of 0.3, 0.5, and 0.7, respectively; when HFNC gas flow was 40 L/min, ΔF_{IO_2} was 0.01, 0.05, and 0.09 at set F_{IO_2} of 0.3, 0.5, and 0.7, respectively.

With a conventional nasal cannula, changes in V_T statistically significantly affected measured F_{IO_2} at all flow levels: At 6 L/min and V_T 300 mL, measured F_{IO_2} was 0.58 ± 0.01, whereas it was 0.40 ± 0 with V_T of 700 mL. There have been other reports that oxygen is delivered more efficiently by high-flow than by low-flow systems.[12,13] Maggiore et al[14] compared 2 high-flow systems on oxygenation for the same set F_{IO_2} after extubation. Compared with the air-entrainment mask, HFNC resulted in better oxygenation, whereas it is unclear whether actual F_{IO_2} was lower with the air-entrainment mask.

Breathing frequency and prong size did not affect measured F_{IO_2}. Similarly, in a previous bench study by Chikata et al[15] on the effect of breathing frequencies and prong size on humidification during HFNC, neither breathing frequency nor prong size influenced humidification during HFNC.

This study has some limitations. Derived from a bench study, the results cannot be directly applied to clinical settings. It only simulated closing of the mouth. Inspiratory time and inspiratory flow were fixed regardless of breathing frequency. In real life, as breathing frequency increases, inspiratory flow increases and inspiratory time decreases.

The present study was, moreover, carried out using only one inspiratory flow waveform, and the nasal prongs were firmly fixed into the modeled external nares. In real life, peak inspiratory flow varies breath-by-breath in each patient, and the position of the prongs frequently varies.

Conclusions

In a bench study, during HFNC, we investigated measured F_{IO_2} under various spontaneous breathing conditions and with different prong sizes. When HFNC gas flow was less than 40 L/min, measured F_{IO_2} was affected by high V_T. HFNC gas delivery, however, was much less affected by changes in V_T than was conventional nasal cannula delivery.

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