Oxygen Injection Site Affects F_{IO_2} During Noninvasive Ventilation

Bing Dai MD, Jian Kang MD, Na Yu MD, Wei Tan, and Hong-Wen Zhao MD

BACKGROUND: Most portable bi-level positive airway pressure devices are not equipped with air-oxygen blenders for precisely regulating oxygen concentrations, and supplemental oxygen must be added to increase the F_{IO_2}. Very few studies have investigated the factors that affect F_{IO_2}, and their conclusions have been inconsistent. We investigated in vitro noninvasive ventilation (NIV) parameters and their effects on F_{IO_2}, particularly the effect of the oxygen injection site. METHODS: NIV was simulated with a test lung and manikin setup. F_{IO_2} was measured with 4 oxygen injection sites (mask, in front of the exhalation valve, at the humidifier outlet, and proximal to the ventilator), with 3 exhalation valve types, with 2 oxygen flows, and with 4 combinations of inspiratory and expiratory pressure. RESULTS: Oxygen flow, inspiratory and expiratory pressure, and exhalation valve type all affected F_{IO_2}. For a given oxygen flow, the oxygen injection site was the most important factor that affected F_{IO_2}. The oxygen injection site that was closest to the patient (on the mask) had the higher F_{IO_2} ($P < .001$). CONCLUSIONS: The oxygen injection site had the greatest effect on F_{IO_2} during NIV. *Key words: F_{IO_2}; noninvasive ventilation; respiratory flow; oxygen injection site.* [Respir Care 2013;58(10):1630–1636. © 2013 Daedalus Enterprises]

Introduction

The use of noninvasive ventilation (NIV) has increased dramatically during the last 10 years.[1-3] NIV is an effective therapy for treating acute respiratory failure that can arise during exacerbation of chronic obstructive disease or acute cardiogenic pulmonary edema, and in immunocompromised patients. NIV is also a means of weaning patients from endotracheal intubation.[1-3] Ventilator support provides relief for respiratory muscles, increases ventilation, reduces dyspnea and breathing frequency, and improves arterial oxygenation.[1]

Most patients on NIV require supplemental oxygen, but many specialized ventilators for NIV are not equipped with air-oxygen blenders for precisely regulating F_{IO_2}, so ensuring the appropriate F_{IO_2} can be difficult.[4-6]

Numerous factors affect F_{IO_2}, and the interactions among these factors are complex. Patient factors include respiratory drive, breathing frequency, airway resistance, and lung compliance. Ventilator factors include oxygen flow, inspiratory/expiratory pressure, and the oxygen injection site. Clinically controllable factors are often chosen based on the experience of the medical staff, such as the oxygen injection site and the exhalation valve. Very few studies have investigated what factors influence F_{IO_2} during NIV, and some of their conclusions have been inconsistent, particularly with regard to oxygen injection site.[7-10] This was possibly due to different experimental designs (human vs in vitro studies) and/or using different types of equipment, particularly with regard to the response times of the oxygen sensors. No studies have investigated the extent to which these factors affect the F_{IO_2} that can be delivered.

We performed in vitro experiments to investigate the effects of oxygen flow, oxygen injection site, inspiratory/expiratory pressure, and type of exhalation valve on F_{IO_2} during NIV. We used an oxygen sensor with a rapid response time (300 ms) and software of our design, which provided better accuracy of F_{IO_2} measurement than had previous studies.

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The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.02172

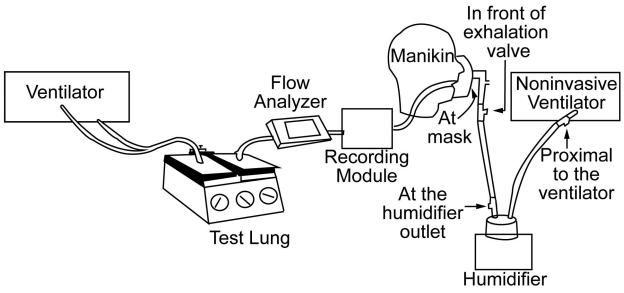

Fig. 1. Experimental setup.

QUICK LOOK

Current knowledge

Ventilators designed for noninvasive ventilation typically do not provide precise control of F_{IO_2}. A low flow of oxygen bled into the inspiratory limb is commonly used, but this method results in variable F_{IO_2}, based on type of ventilator, site of oxygen delivery, and circuit configuration.

What this paper contributes to our knowledge

Oxygen flow, set inspiratory and expiratory pressure, and the type of exhalation valve all affected F_{IO_2}. The site of oxygen delivery into the circuit was the most important factor. Oxygen delivery closer to the patient gave the highest F_{IO_2}.

Methods

Simulation Lung Platform

For the simulation experiments we used a dual-chamber test lung (Training and Test Lung 1600, Michigan Instruments, Grand Rapids, Michigan). As shown in Figure 1, the driver chamber was connected to a ventilator (PB840, Puritan Bennett/Covidien, Mansfield, Massachusetts). The test chamber was connected to a portable bi-level positive airway pressure (BPAP) device (Synchrony, Respironics, Andover, Massachusetts), and the face mask was applied to a manikin head via a 1.8 m one-way ventilator circuit (312107, Respironics, Andover, Massachusetts). The connections between the tubing and mask were tight, and the junctions between the face mask and manikin head were filled with silicone patches. The ventilator circuit had no unintentional leaks.

A gas analyzer (VT-Plus, Fluke, Everett, Washington) and a recording module of our design were connected in series with the ventilator circuit between the face mask and the test lung. The ventilator circuit was attached to an empty humidifier canister.

Rhythmical changes in the driver chamber volume that simulated spontaneous human breathing were transmitted to the test chamber through a metal rod. The driver chamber triggered the ventilator during early inspiration. Once a breath was triggered, test chamber inflation was controlled by pre-set parameters. No auto-triggering or missed triggers occurred in any of the experiments. Compliance was set at 0.05 L/cm H_2O, and resistance was set at 5 cm H_2O/L/s, with a parabolic airway resistor (Pneuflo Rp5, Michigan Instruments, Grand Rapids, Michigan, which has a resistance of 4.3 cm H_2O/L/s at a flow of 60 L/min). An oxygen flow meter was connected to a 50 psi wall oxygen source, and oxygen was delivered at 4 different sites, through an extension tube with a 3-way adapter.

Experimental Conditions

The ventilator was set in the volume control mode (tidal volume 500 mL, peak flow 50 L/min, square waveform). The portable BPAP device was set in the spontaneous breathing mode, with a pressure rise setting of 3. In all the experiments the PEEP level of the ventilator was maintained at the same expiratory pressure as the BPAP device, to ensure simultaneous triggering.

The inspiratory and expiratory pressures from the BPAP device were 15/5, 15/10, 25/5, and 25/10 cm H_2O. The exhalation valves included a single-arch valve (Respironics, Andover, Massachusetts), a plateau exhalation valve (PEV, Respironics, Andover, Massachusetts), and a mask valve (leak port in the mask) (Respironics, Andover, Massachusetts). The tested oxygen flows were 5 and 10 L/min. The oxygen injection sites were proximal to the ventilator, at the humidifier outlet, proximal to the exhalation valve, and on the mask.

Oxygen Concentration Measurements

Prior to each experiment, to reduce error and ensure experimental reproducibility, the gas analyzer recorded baseline fluctuations in flow and pressure. Each time an experimental condition was changed, the measurements were compared with the baseline fluctuation range. If the difference was too large, the cause of the difference was corrected and the measurements were taken again. For each new experimental condition, a minimum of 3 min of stabilization time was included prior to the next F_{IO_2} measurement.

Oxygen concentration was measured with an oxygen sensor (OOM109/OOM109-LF2, EnviteC, Wismar/Honeywell, Morristown, New Jersey), with which the response time for a 90% change is 300 ms. Inspiratory flow was continuously monitored with a flow sensor at a sampling frequency of 30 ms. The inspiratory phase was identified

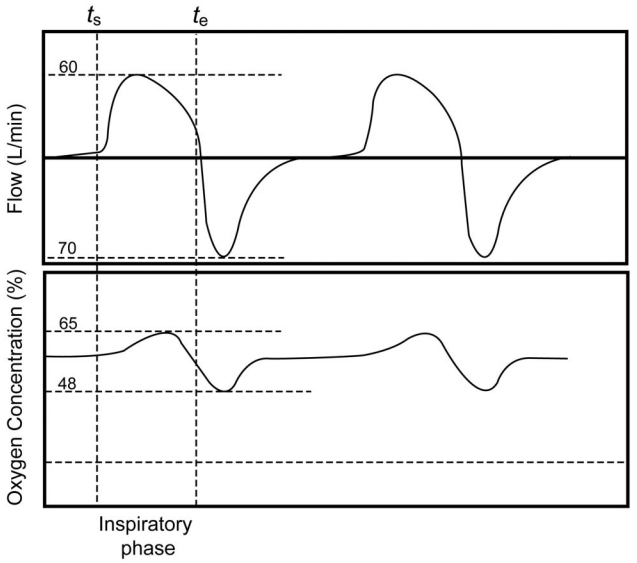

Fig. 2. Example flow/time curve and oxygen concentration curve.

from the flow waveform. Software of our design was used to multiply the oxygen concentration by the inspiratory flow at each sampling point of the inspiratory phase. The delivered oxygen volume and the tidal volume were determined by mathematical integration. The delivered oxygen volume was divided by the tidal volume to determine F_{IO_2}. F_{IO_2} of the inspiratory phase was calculated using data from 3 breathing cycles under the various experimental conditions, with the equation:

$$F_{IO_2} = \frac{\dot{V}_{O_2} \int_{ts}^{te} V(t)\, O_2\%(t)\, d(t)}{Vt = \int_{ts}^{te} V(t)\, d(t)} \times 100\%$$

in which V(t) is the volume of a given sampling time point (d(t)), $O_2\%(t)$ is the O_2 percentage of a given d(t), t_e is the ending time point, and t_S is the starting time point.

Statistical Analysis

The F_{IO_2} results are given as mean ± SD. Comparisons of the F_{IO_2} data were made by analysis of variance, with a Bonferroni correction for type 1 error adjustment

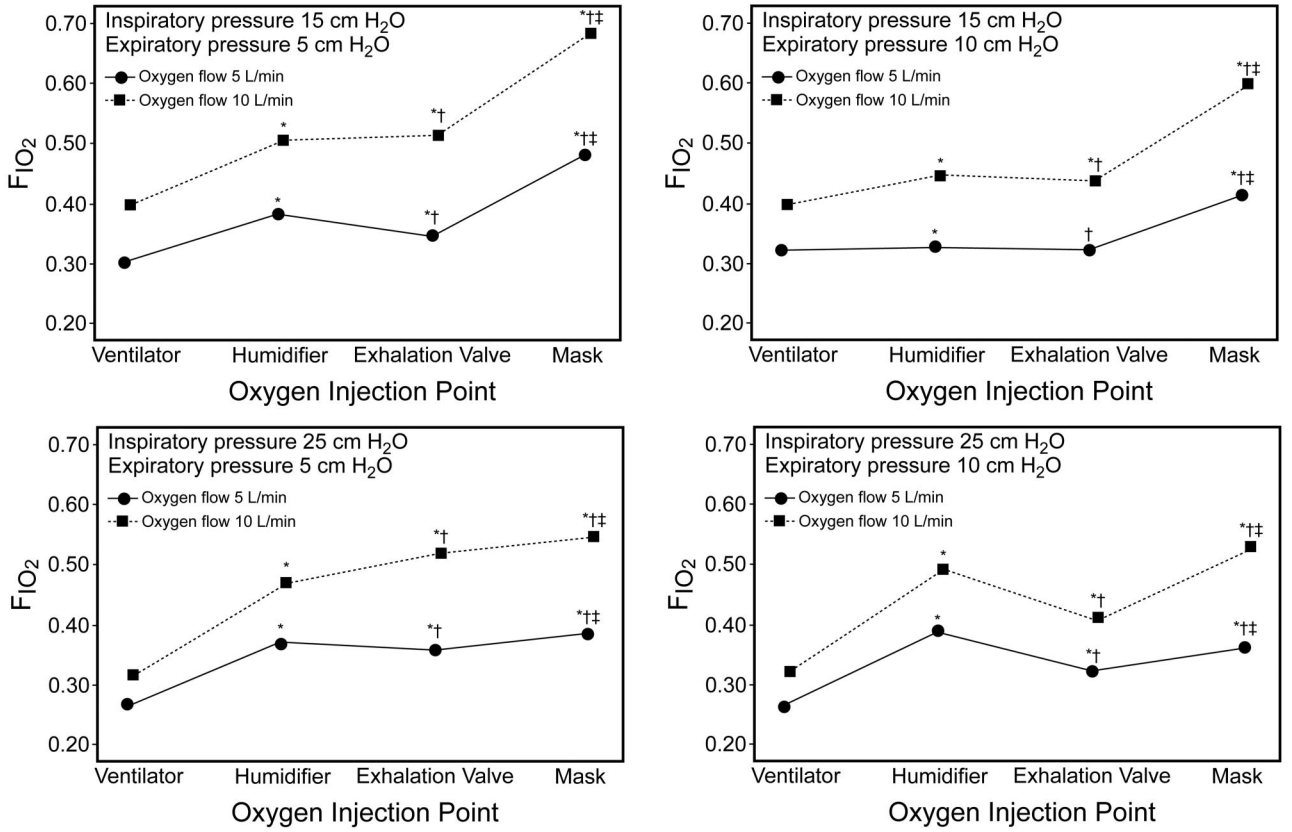

Fig. 3. Mean F_{IO_2} with the single arched valve. * $P < .05$ compared to proximal to ventilator. † $P < .05$ compared to at the humidifier. ‡ $P < .05$ compared to in front of the exhalation valve.

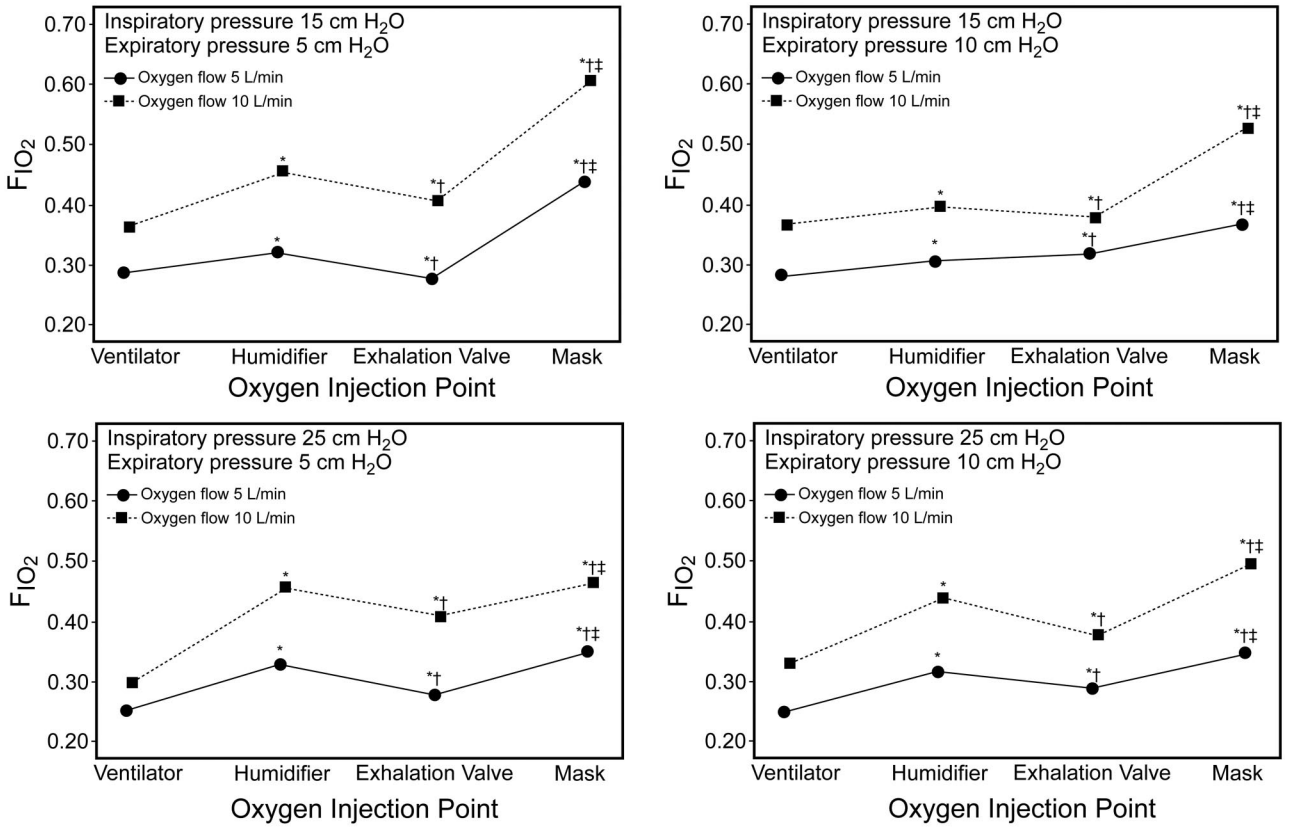

Fig. 4. Mean F_{IO_2} with the plateau exhalation valve. * $P < .05$ compared to proximal to ventilator. † $P < .05$ compared to at the humidifier. ‡ $P < .05$ compared to in front of the exhalation valve.

when multiple comparisons were made. A general linear model was used to assess the effect of each experimental factor on F_{IO_2}, after adjusting for other experimental factors. The adjusted mean differences and corresponding 95% CIs were calculated from the general linear model. We assessed the independent contribution of each experimental factor on F_{IO_2} with F tests, using type III sums of squares. The statistical analyses were done with statistics software (SAS 9.2, SAS Institute, Cary, North Carolina). A 2-tailed P value of $< .05$ was considered significant.

Results

Figure 2 shows an example flow/time curve and oxygen concentration curve. Figure 3 shows the F_{IO_2} results with the single arched valve. Figure 4 shows the F_{IO_2} results with the plateau exhalation valve. Figure 5 shows the F_{IO_2} results with the mask valve.

The average F_{IO_2} differed significantly among the 4 oxygen injection sites (all $P < .001$). The highest average F_{IO_2} was with the oxygen injected at the mask, except for with the single arched valve at 25/10 cm H_2O and oxygen flow of 5 L/min.

The Table summarizes the effects of these different factors on F_{IO_2} during simulated NIV. After adjusting for the other factors, the mean F_{IO_2} values were significantly increased with a higher oxygen flow (10 L/min vs 5 L/min, increased 48.5%, adjusted mean difference 11.05, 95% CI 10.28–11.81, $P < .001$), a lower inspiratory pressure (15 cm H_2O vs 25 cm H_2O, increased 13.3%, adjusted mean difference 3.03, 95% CI 2.27–3.79, $P < .001$), and a lower expiratory pressure (5 cm H_2O vs 10 cm H_2O, increased 11.3%, adjusted mean difference 2.57, 95% CI 1.81–3.33, $P < .001$), the use of a single-arch valve (compared to at the mask valve, increased 9.6%, adjusted mean difference 2.19, 95% CI 1.26–3.13, $P < .001$), and when the oxygen injection site was at the mask (compared to proximal to the ventilator, increased 70.2%, adjusted mean difference 15.99, 95% CI 14.91–17.07, $P < .001$).

Based on comparisons by F tests, using type III sums of squares, all 5 of these experimental factors had significant effects on F_{IO_2}, after adjusting for other experimental factors (all $P < .001$). Moreover, among these 5 factors, the oxygen injection site had the greatest effect on F_{IO_2}, followed by oxygen flow, type of exhalation valve, inspiratory pressure, and expiratory pressure.

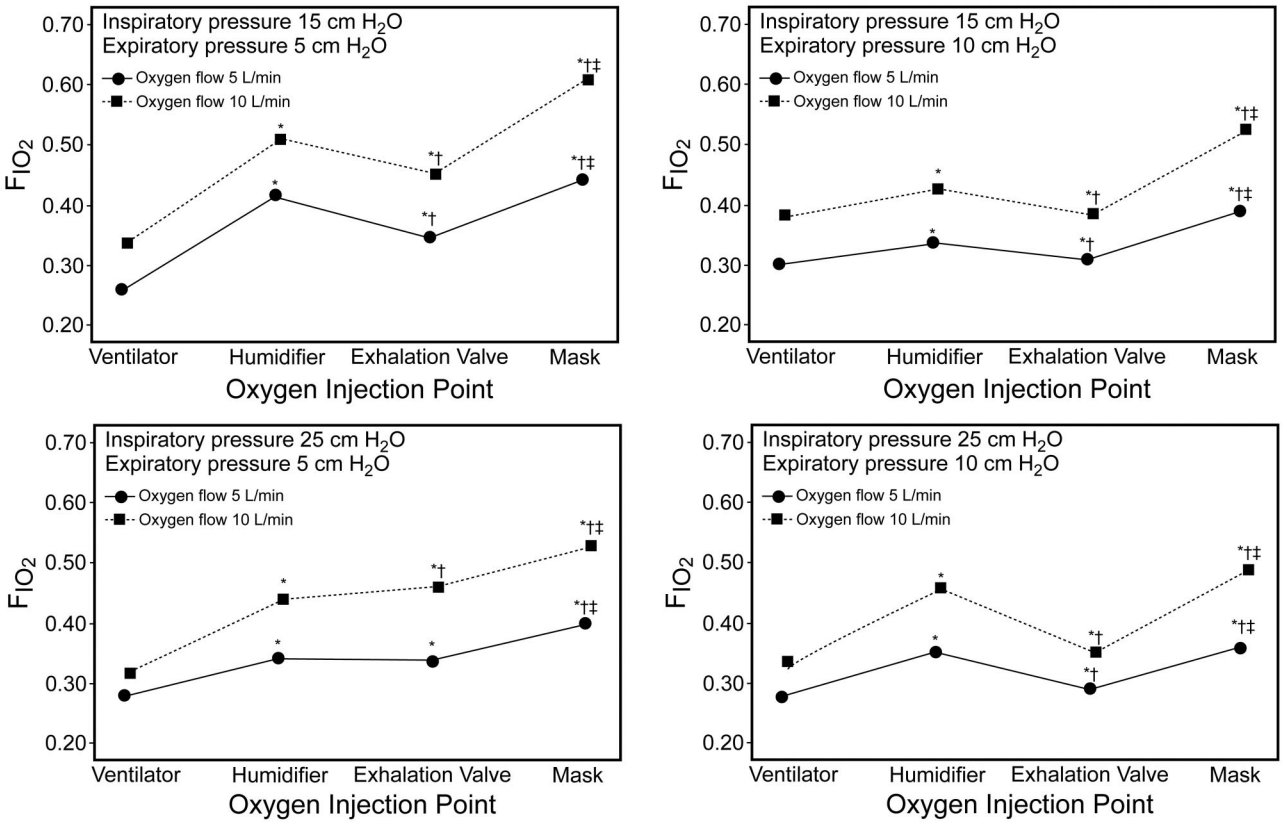

Fig. 5. Mean F_{IO_2} with the mask valve. * $P < .05$ compared to proximal to ventilator. † $P < .05$ compared to at the humidifier. ‡ $P < .05$ compared to in front of the exhalation valve.

Table. Experimental Factor Effects on F_{IO_2} During Simulated Noninvasive Ventilation, Assessed Using General Linear Models

	Adjusted Mean Difference*	95% CI
Oxygen flow (reference 5 L/min)		
10 L/min	11.05	10.28 to 11.81
Inspiratory pressure (reference 25 cm H_2O)		
15 cm H_2O	3.03	2.27 to 3.79
Expiratory pressure (reference 10 cm H_2O)		
5 cm H_2O	2.57	1.81 to 3.33
Exhalation valve (reference mask valve)		
Plateau exhalation valve	−2.04	−2.98 to −1.11
Single-arch valve	2.19	1.26 to 3.13
Oxygen injections site (reference proximal to ventilator)		
Humidifier outlet	9.10	8.03 to 10.18
In front of exhalation valve	5.81	4.73 to 6.89
Mask	15.99	14.91 to 17.07

* Adjusted mean difference in F_{IO_2} compared to the reference, controlled for other experimental factors. All P values $< .001$.

Discussion

Clinically, supplemental oxygen is often added to the NIV circuit to maintain the hemoglobin oxygen saturation level at > 90% for patients with acute respiratory failure.[1] Multiple factors affect F_{IO_2}. We found that the oxygen injection site remarkably affected F_{IO_2}: for a given oxygen flow, the oxygen injection site had the greatest effect on

F_{IO_2}, and the oxygen injection site closest to the patient (at the mask) had the highest F_{IO_2}. The lowest F_{IO_2} was when oxygen was added proximal to the ventilator. The higher F_{IO_2} may have been due to a lack of oxygen leak through the exhalation port before the inspired gas reached the mask. A higher oxygen flow also increased F_{IO_2}. The type of exhalation valve also affected F_{IO_2}.

Waugh and De Kler[9] found the highest F_{IO_2} when oxygen was added at the ventilator outlet; however, they only used a mask valve. Also, their in vitro model was a passive analog lung NIV, which could not simulate spontaneous breathing, and they used pressure control ventilation, which is different from NIV with pressure support ventilation.

Schwartz et al[8] found that the type of exhalation valve affected F_{IO_2}. F_{IO_2} was greater when oxygen was added proximal to the ventilator with the leak port located in the mask, or when oxygen was added to the mask and the leak port was in the respiratory circuit. However, Schwarz et al used a mask valve that was different from ours, and may have reduced the actual delivered F_{IO_2}. Also, their oxygen sensor had a much slower response time (30 s) for a 90% change than did ours (300 ms).

Thys et al[7] also found that adding oxygen between the patient and the exhalation valve resulted in a lower F_{IO_2} than adding oxygen between the exhalation valve and the ventilator. However, Thys et al studied human subjects, so they could not determine when oxygen was added to the mask and the actual F_{IO_2} delivered to the subject. They also used an oxygen sensor with a slow response time. Yet their F_{IO_2} was higher at lower inspiratory (15 cm H_2O) and expiratory (5 cm H_2O) pressures[7-9] and at a higher oxygen flow.[7,9] In practice, the oxygen injection site should be selected based on the clinical situation. For example, an oxygen tube can easily fall off if oxygen is injected into a mask, and a specialized adapter is needed when oxygen is added at a humidifier outlet.

In previous studies[6-10] the oxygen sensor response times for a 90% change were slow (12–43 s), and those studies did not distinguish between the inspiratory phase and the expiratory phase. F_{IO_2} is relatively low at the beginning of the inspiratory cycle, while the inspiratory flow is high, whereas oxygen concentration is highest at the end, while the inspiratory flow is lowest, with less efficient oxygen delivery. Our oxygen sensor's fast response time and the software of our design allowed us to more accurately measure the F_{IO_2}.

One difficulty with measuring the actual delivered oxygen concentration is rebreathing of mixed inhaled and exhaled gases. The standard single-limb BPAP circuit increases the likelihood of rebreathing.[11] To lessen this effect, we used a condition that minimizes rebreathing: a medium-size mask with expiratory pressure set at 5 cm H_2O.[12] Even so, rebreathing could affect the F_{IO_2}, which was one limitation of our study.

Our intent was not to predict precise oxygen concentrations for all parameters. Rather, we wanted to systematically test the general effects of these variables to estimate conditions that would be relevant for patients: that is, controllable NIV circuit variables that can most affect oxygen delivery and may help us distinguish a patient's increased oxygen needs due to worsening illness or other factors that affect F_{IO_2}. Although noninvasive ventilators with oxygen blenders are not popular in China, many patients in the acute phase can only use alternatives to these noninvasive ventilators, without oxygen blender. We should regard noninvasive ventilator with oxygen blender as the first choice in those patients. Low-flow oxygen and pressures in the range of 20 cm H_2O are reasonably safe, whereas with higher flow and high pressure the margin of error increases. This is more likely to occur in the acute phase, in patients in the medical, surgical, and emergency departments where such ventilators have seldom been used.

As shown in Figure 3, in our general linear model the largest effect was from the oxygen injection site (for a given oxygen flow). In addition, our fast-response oxygen sensor and software should be readily applicable to other studies in which oxygen concentration varies rapidly. Additionally, for oxygen bottles or oxygen concentrators that are used as oxygen sources in the patient's home, the user can conserve oxygen by selecting a suitable oxygen injection location. This is a very important application for home NIV.

Conclusions

The site of oxygen delivery into the NIV circuit, the type of exhalation mask, the oxygen flow, and the inspiratory and expiratory pressures affected the F_{IO_2}. Among all the variables we examined, for a given oxygen flow, the oxygen injection site had the most significant effect on the F_{IO_2} during NIV. Oxygen injection site is a clinically controllable variable and should be given more consideration during NIV.

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