Influence of Leakage from Non-Invasive Positive Pressure Ventilation Mask on FiO$_2$ Value Delivered by Home Oxygen Therapy Concentrator: A Bench Study on Simulating Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Introduction: During the application of non-invasive positive pressure ventilation (NPPV) therapy in home mechanical ventilation (HMV), leaks in the NPPV mask may occur owing to the position of the mask due to conditions such as skin disorders. Methods: To investigate whether such a leak affects FiO$_2$ supplied to the alveoli, we simulated a patient with chronic obstructive pulmonary disorder during NPPV in HMV. In addition, FiO$_2$ was measured in the portion assumed to be the mouth and lungs while setting the flow of the oxygen concentrator and leak amount based on a previous study. Results: FiO$_2$ supplied to the lungs increased statistically significantly upon increasing the amount of leak ($P < 0.001$). Moreover, values measured for the mouth were similar. However, our results were different from those of a previous study. Conclusions: We observed that FiO$_2$ supplied to alveoli can be reduced by a leak in the NPPV mask. Because our results differ from those previously reported, we believe that further studies should reassess the selection of respirators and oxygen concentrators.
1. Introduction

In recent years, the application of noninvasive positive pressure ventilation (NPPV) therapy in home mechanical ventilation (HMV) has increased [1]. In particular, NPPV is useful for patients with chronic obstructive pulmonary disease (COPD) [2] [3], which is treated with long-term home oxygen therapy (HOT) [4]. NPPV therapy may confer therapeutic effects, such as a reduction in respiratory work, sustained improvement of arterial blood gas status, reduction in hospitalization frequency, and improved survival and quality of life [5]. In addition, in NPPV therapy, ventilation is performed using a mask without tracheal intubation; thus, NPPV therapy facilitates the ability to have conversations and eating, and has benefits such as a lower risk of infection. However, as a condition for obtaining a therapeutic effect, it is imperative to fit the mask to the patient.

In NPPV, in contrast to intermittent positive-pressure ventilation (IPPV), FiO₂ depends upon complex factors such as the amount of ventilation and leak that is associated with patients in addition to the devices [6]. A study reported that leaks in the mask may occur because of altered positioning of the mask resulting from a skin disorder or selection of an inappropriate mask on NPPV enforcement [7]. Leaks around the mask can compromise the effectiveness of NPPV, but NPPV ventilators can compensate for leaks [8]. However, when HOT device and NPPV therapy are used in combination, since the ventilator and HOT device are independent circuit configurations, it is difficult to compensate for the loss in oxygen concentration in the air taken in due to the leak (Figure 1). Therefore, in this study, we simulated lungs of COPD patients to determine the extent to which FiO₂ supplied to the alveoli can be affected by the reduction in oxygen concentration due to a leak in the mask.

2. Methods

2.1. Experimental Materials and Methods

We had to provide spontaneous respiration because we simulated COPD patients in this study. We used the following method, as described in a previous study [9]. First, the left lung of the TTL model lung (Training and Test Lung®, Michigan Instruments, Kentwood, MI, USA) was used to produce mandatory ventilation, and the right lung provided an inspiratory effort. Spontaneous respiration can be produced by attaching a lift bar between the left and right lungs. Mandatory ventilation of the left lung was performed using LTV-1000 (Pacific Medico, Tokyo, Japan). The ventilator was set in pressure-control continuous
Figure 1. Circuit diagram. To simulate the NPPV mask, we developed an adapter with an O₂ supply port and a leak port attached between the inspiration side circuit of VELA and Y piece. Through this adapter, O₂ was supplied to the TTL model lungs and leaked. The left side of the figure of the TTL model lung represents the left lung, the right represents the right lung. Circuit diagrams show HOT only (a), using VELA without leakage (b), and spontaneous respiration with leakage (c).
mandatory ventilation (PCV-CMV) mode, spontaneous respiration was set at 12 times, inspiratory pressure was set at 15 cmH₂O, and inspiratory time was set at 1 sec. In the right lung, spontaneous respiration was enabled using VELA (Care Fusion 207, Palm Springs, CA, USA) to simulate respiration in patients with COPD. VELA was set in the NPPV-pressure support ventilation (PS) mode. PS was set at 10 cmH₂O, positive end-expiratory pressure (PEEP) was set at 5 cmH₂O, and the flow trigger was set at 2 L/min. Airway resistance in the left lung of the TTL model lung was set at 20 cmH₂O to produce spontaneous respiration, and compliance was set at 0.05 L/cmH₂O. Airway resistance in the right lung of the TTL model lung was set at 50 cmH₂O to simulate lungs of patients with COPD, and compliance was set at 0.04 L/cmH₂O. To simulate the leaks from NPPV mask, we developed an adapter with an O₂ supply port and a leak port, and attached it between the inspiration side circuit of VELA and the Y piece. Through this adapter, O₂ was supplied to the right lung of the TTL model lungs and leaked (Figure 1).

2.2. Method of FiO₂ Measurement Simulating No Air Leak Using HOT Device and VELA

For HOT, an oxygen concentrator (O₂ Green SHIZUNE IT-5 L, TERUMO, Japan) was used. Six flow rates of O₂ (0.5, 1, 2, 3, 4, 5 L/min) in the TTL model lung were used. The oxygen concentration meter was placed at two locations: the right lung of the TTL model lung, which simulated a COPD patient, and the connection port of the circuit (simulated patient mouth), used to measure FiO₂ after 5 minutes. In order to obtain a stable O₂ value, O₂ was passed through the O₂ supply port for 5 minutes. The O₂ measurement was repeated ten times for each flow setting. For the FiO₂ measurement of the simulated patient’s mouth, the combined Y portion was measured using an oxygen concentration meter. Furthermore, after performing the measurements for 5 minutes, in order to eliminate the accumulated O₂, FiO₂ in the left lung of the TTL model lung was released into room air until the O₂ concentration reached 21%, and then O₂ supply was initiated.

2.3. FiO₂ Measurement Method Simulating Air Leak Using HOT Device and VELA

In order to simulate NPPV by VELA, oxygen was supplied from the oxygen concentrator to the lungs of the TTL model lung and at the same time a ventilator was attached. In addition, oxygen at concentrations ranging from 0.5 to 5 L/min was released from the adapter. From the summed-up value of the ventilation volume per minute from the respirator and the oxygen volume per minute in the oxygen concentrator, leaked at 5 L/min, the leak amount was precisely measured using the flow analyzer (PF-300, Ver. 3.1, imt Medical, Switzerland). From there, FiO₂ was measured for 5 minutes in the TTL model lung part and Y piece part. Measurements were repeated 10 times for each setting.
2.4. Statistical Analysis

The FiO₂ measurements using HOT device and VELA simulating each state were compared between three groups of leaks: 0 L/min, 5 L/min, and 10 L/min. For comparison between groups and all variables, multiple comparisons were performed by the Tukey HSD method. Statistical analyses were performed with statistical software “R” (Version 3.5.0, The R Foundation for Statistical Computing, Vienna, Austria), and P < 0.01 was considered statistically significant.

3. Results

When supplying O₂ to the lungs using the oxygen concentrator alone, FiO₂ > 90% was obtained at an O₂ flow rate of 4 - 5 L/min. At an O₂ flow rate of less than 4 L/min, FiO₂ was 88.9% at 3 L/min, 82.3% at 2 L/min, 60.8% at 1 L/min, and 35.9% at 0.5 L/min. When the O₂ flow rate was set at less than 3 L/min, FiO₂ was markedly decreased. Furthermore, when NPPV therapy was used in combination, FiO₂ decreased to 28% to 41% at an O₂ flow rate of 2 to 5 L/min. The largest reduction in FiO₂ using NPPV therapy combined with HOT device was 55.5% at 3 L/min O₂ flow rate (Figure 2).

When leakage was 5 or 10 L/min and O₂ flow rate was 3 to 5 L/min, FiO₂ decreased to 28% to 41% at an O₂ flow rate of 2 to 5 L/min. The largest reduction in FiO₂ using NPPV therapy combined with HOT device was 55.5% at 3 L/min O₂ flow rate (Figure 2).

Figure 2. Variation in FiO₂ with O₂ flow. Using the oxygen concentrator alone, more than 90% of FiO₂ was obtained at an O₂ flow rate of 4 - 5 L/min. At O₂ flow rates of less than 4 L/min, FiO₂ was 88.9% at 3 L/min O₂, 82.3% at 2 L/min O₂, 60.8% at 1 L/min O₂, and 35.9% at 0.5 L/min O₂. When the O₂ flow was less than 3 L/min, FiO₂ markedly decreased. When using a ventilator, the highest reduction in FiO₂ was 55.5% at an O₂ flow rate of 3 L/min.
decreased by approximately 3% in all cases. Thus, when the leakage increased from 0 to 10 L/min, the maximum FiO2 reduction was approximately 6% (Table 1, Figure 3).

However, FiO2 decreased by 2.8% at 1 L/min O2 flow and 1.4% at 0.5 L/min O2 flow when the leakage was increased from 0 to 10 L/min. At low rates of O2 flow, FiO2 was minimally affected by the leakage (Table 1, Figure 3).

These results revealed a marked difference between each leak amount, and

Table 1. Estimation of FiO2 in lungs imitating an NPPV mask leak.

<table>
<thead>
<tr>
<th>Leak [0 L/min]</th>
<th>Leak [5 L/min]</th>
<th>Leak [10 L/min]</th>
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<tr>
<td>0.5</td>
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</tr>
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<tr>
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</tr>
<tr>
<td>5</td>
<td>41.5</td>
<td>5</td>
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</table>

Figure 3. Comparison of FiO2 with changes in leakage and O2 flow. When comparing 5 and 10 L/min rates of leakage with 3 and 5 L/min O2 flows, we observed that FiO2 decreased by approximately 3% in both leakage cases. Thus, when the leakage increased from 0 to 10 L/min, a maximum reduction of approximately 6% of FiO2 occurred. However, FiO2 decreased by 2.8% at 1 L/min O2 flow and 1.4% at 0.5 L/min O2 flow when the leakage increased from 0 to 10 L/min. At low rates of O2 flow, FiO2 was not markedly affected by leakage.
indeed, there was a significant difference in FiO\textsubscript{2} (P < 0.001) (Table 1, Figure 3).

4. Discussion

This study differs from previous study by Goutorbe et al. (2013) in two respects. First, HOT device has not been used in the previous study, but in this study, HOT device was used to measure lung oxygen concentration. Second, in the previous study, an oxygen cylinder was connected to the ventilator, but in this study, oxygen concentration was measured by connecting the HOT device to the respiratory circuit instead of the ventilator. Here, it is worthwhile to note that in Japan, oxygen therapy at home is performed using NPPV therapy and HOT device in combination, and the HOT device is connected to a ventilator circuit.

Three noteworthy points were confirmed in this study. First, the FiO\textsubscript{2} value when using NPPV therapy and HOT device was clearly lower than the FiO\textsubscript{2} value using only HOT device. The difference was the maximum when the O\textsubscript{2} flow rate was 3 L/min. Second, upon setting the O\textsubscript{2} flow rate at less than 1 L/min, the FiO\textsubscript{2} value markedly decreased. Third, the FiO\textsubscript{2} value decreased as the leak amount increased. This phenomenon has not been observed in the previous study.

Regarding the first observation, at an O\textsubscript{2} flow rate of 5 L/min and using only HOT device, the FiO\textsubscript{2} was 93%, and a difference of approximately 51% was observed compared to the measurement obtained using a mechanical ventilator with HOT device. A maximum difference of about 55% was observed at a flow rate of 3 L/min. When O\textsubscript{2} was delivered in combination with a ventilator in a previous study, FiO\textsubscript{2} was approximately 39% in the absence of leakage and at an O\textsubscript{2} flow rate of 4 L/min. In the present study, the FiO\textsubscript{2} was approximately 38%, which is not a substantial difference. However, it is important to note that a maximum reduction in FiO\textsubscript{2} of 55.5% is observed when using HOT device with a mechanical ventilator, with an O\textsubscript{2} flow rate of 3 L/min or more, as compared to the FiO\textsubscript{2} obtained when HOT device is used alone.

Regarding the second observation, in addition to the performance of the adsorptive oxygen concentrator, the maximum ventilation volume of the TTL model lung is thought to be related to the performance. Because the maximum ventilation volume of the TTL model lung used in this study was 2 L, when the O\textsubscript{2} flow was set to less than 1 L/min, the lungs were not sufficiently filled with oxygen, as measured at 5 minutes. Therefore, it is thought that FiO\textsubscript{2} was markedly reduced at O\textsubscript{2} flow of less than 1 L/min. When we set the O\textsubscript{2} flow at 1 L/min and measured FiO\textsubscript{2} for 30 minutes twice, then similar values were obtained compared with measurements recorded for 5 minutes. Thus, we found that the FiO\textsubscript{2} concentration was difficult to increase in the simulated lung at an O\textsubscript{2} flow rate of less than 1 L/min. In the guidelines for respiratory therapy, it remains unclear how much FiO\textsubscript{2} decreases when a mechanical ventilator is added to an oxygen concentrator.

As regards the third observation, this difference is thought to be due to the
difference in the mode of oxygen supply. In the previous study, an oxygen cylinder was used, and O₂ was mixed directly from a ventilator and sent to the simulated lung. Therefore, FiO₂ increased despite the rate of leakage increasing from 5 to 10 L/min, at O₂ flow rates of 1, 2, and 4 L/min. This is considered to be a problem when the leak amount is adjusted. Although an effect of the leak on FiO₂ has been reported previously by Miyoshi et al. (2005), the reduction in FiO₂ when using HOT device has not yet been clarified. Furthermore, in the study by Goutorbe et al. (2013), the increase in FiO₂ with an increase in the leak amount could not be confirmed. By contrast, in this study, we mainly considered home care in Japan, so we used HOT device to supply O₂ to the middle of the inspiratory side circuit of VELA. In this research method, it is considered that the cause of O₂ decrease that cannot be compensated by the leakage from the HOT device occurs due to the difference in the method of mixing air and O₂. Therefore, it was found that when the O₂ flow rate was 3 L/min or more, FiO₂ decreased by about 6% as the leakage increased at this flow rate (Table 1).

O₂ is supplied through a piping in the clinical setting. In our study, O₂ was supplied from HOT device because there is no oxygen piping facility at home. In a previous study, O₂ was supplied on the same principle as piping from a ventilator [9]. This is an indicator when using respiratory equipment in the hospital. We believe that this research provides very useful and important knowledge for home medical applications.

In our study, important findings on the use of HOT device in combination with a ventilator have been reported, but there are some limitations to this study. First, we simulated COPD patients using TTL model lungs, but we have not studied this phenomenon in humans. Therefore, inter-individual differences such as gender and physical differences were not reflected in the reduction of FiO₂. We expect to obtain more robust results in future by conducting the same experiments on humans and increasing the sample size.

Second, errors in FiO₂ measurement may occur due to the performance of the ventilator. Currently, there are many types of ventilators used at home care, and the performance of the equipment varies from manufacturer to manufacturer. Future research is warranted to identify the correct FiO₂ value by performing a number of validation experiments using various types of ventilators. Third, even for the same ventilator, it is necessary to compare the difference between FiO₂ supplied from oxygen piping and FiO₂ supplied from HOT device. In the previous study, the measurement was based on the former method, so the result showed that FiO₂ increased at a leakage rate of 10 L/min compared to a leakage rate of 5 L/min. In this study, different findings were obtained using the latter method. This may have been caused by different oxygen supply methods. We believe that this discrepancy can be resolved by performing more comparative experiments. Our current research provides scientific evidence to obtain multiple measurements of FiO₂ reduction caused by leaks when using HOT device in the future.
5. Conclusion

In this study, we observed that FiO₂ decreases because of a leak in the NPPV mask. Moreover, we measured the FiO₂ for each oxygen flow rate supplied from the oxygen concentrator and the reduction in FiO₂ with the use of a mechanical ventilator. However, our results differ from those of a previous study; therefore, we believe that further studies should be conducted using the same method of oxygen supply as that used in the previous study. To elucidate these differences, it will be important to reconsider the selection of respirators and oxygen concentrators.

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