A New Formula for Predicting the Fraction of Delivered Oxygen During Low-Flow Oxygen Therapy

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BACKGROUND: During O2 therapy at low flow in patients who breathe spontaneously, the fraction of delivered O2 (Fdo2) is unknown. In recent years, Fdo2 prediction formulas have been proposed. However, they do not take into account the effect of inspiratory flow (Vi) on the Fdo2. The aim of this study was to validate a new Fdo2 prediction formula, which takes into account the Vi and compares it with other Fdo2 prediction formulas. METHODS: During a bench study, spontaneous breathing was generated with a mechanical test lung connected to a mechanical ventilator set to volume control mode. O2 flow from a wall-mounted tube was delivered through a heat-and-moisture exchanger filter. A flow sensor recorded each breath of the Vi in ambient temperature and barometric pressure conditions. Three parameters [O2 flow at 2, 3, 4, 5, 6 L/min; minute ventilation at 5, 10, 15, 20 L/min; and ratio of the inspiratory time (Ti) to the total breathing cycle time (Ttot) (Ti/Ttot value)] were modified to generate many ventilatory patterns. An O2 analyzer continuously examined the Fdo2. RESULTS: When the O2 flow and/or Ti/Ttot increased, the Fdo2 increased. When the minute ventilation increased, the Fdo2 decreased. The results of the Bland-Altman method for the Fdo2 calculated by using our mathematical model and the measured Fdo2 showed that the mean ± SD bias value was equal to 1.49 ± 0.84%, and the limits of agreement ranged from -0.17% to 3.14%. The intraclass correlation coefficients were 0.991 for Ti/Ttot = 0.33 and 0.994 for Ti/Ttot = 0.50, and the coefficient of variation was 2.1% for Ti/Ttot = 0.33 and 1.3% for Ti/Ttot = 0.50. The results of the Bland-Altman method for the Fdo2 calculated by using the Shapiro formula and the Fdo2 measured on the bench indicated that the bias value was 0.075 ± 8.66% and the limits of agreement ranged from -16.89% to 17.04%. For the Vincent formula, the bias value was 3.08% ± 8.56% and the limits of agreement ranged from -13.69% to 19.84%. CONCLUSIONS: The Vi has a major impact on Fdo2 during O2 therapy at low flow. Fdo2 comparisons between frequently used prediction formulas and Fdo2 measured on the bench indicated greater differences. Uncritical use of these formulas should be used cautiously to predict Fdo2. In this study, our prediction formula indicated a good accuracy for predicting Fdo2 during supplemental oxygenation through a heat-and-moisture exchanger in patients who breathe spontaneously. Key words: oxygen; Fdo2; low flow; oxygen therapy; prediction formula. [Respir Care 2018;63(12):1528–1534. © 2018 Daedalus Enterprises]

Introduction

When trying to wean the patient from mechanical ventilation, spontaneous breathing trials assess the patient’s ability to breathe while receiving no ventilatory support. In general, these patients receive oxygen to avoid hypoxemia. During this period, the fraction of delivered O2 (Fdo2) must be maintained within strict limits to avoid arterial
oxygen variations. However, as reported by several studies, the F DO₂ varies according to the O₂ flow and/or the patient’s respiratory pattern (eg, frequency, tidal volume). This raises the question about FDO₂ prediction in patients who are intubated or tracheotomized oxygenated patients who breathe spontaneously with a Heat Moisture Exchanger (HME). In recent years, F DO₂–validated formulas have been promoted. However, they only take into account the administered O₂ flow and are only applicable in resting adult patients who breathe spontaneously and are oxygenated through a nasal cannula, transtracheal catheters, or a tracheostomy or endotracheal tube.

Moreover, these formulas do not take into account the influence of the inspiratory flow (V̇I) on the variability of FDO₂ when the patient receives O₂ at low flow. Our hypothesis is that the V̇I has a major impact on FDO₂ during O₂ therapy at low flow and that these formulas are not accurate in clinical situations. The aim of this study was to validate a new F DO₂ prediction formula that takes into account the V̇I and compares it with other formulas for use in patients who were tracheostomized or intubated and spontaneously breathing.

Methods

Part 1

The following F DO₂ prediction formula was developed (F DO₂ calculated [see the supplementary materials at http://www.rcjournal.com]) and compared with the F DO₂ measured in a bench study (F DO₂ measured).

\[ F_{DO_2} = 0.21 + (x) \times \frac{L/min O_2}{x} = \begin{cases} 1/(4 \times V̇E) & \text{for } T_I/T_{tot} = 0.33 \\ 1/(2.5 \times V̇E) & \text{for } T_I/T_{tot} = 0.50 \end{cases} \]

with O₂ flow in L/min, minute ventilation (V̇E) in L/min, inspiratory time (T_I) in seconds; and total inspiratory and expiratory time (T_{tot}) in seconds.

QUICK LOOK

Current knowledge

During O₂ therapy at low flow when using a heat moisture exchanger, the fraction of delivered O₂ (F DO₂) can be estimated with prediction formulas. However, these formulas do not consider the effect of inspiratory flow on F DO₂. The true F DO₂ delivered in these cases is not precisely known.

What this paper contributes to our knowledge

Comparisons with prediction formulas typically used by clinicians show major differences between the F DO₂ calculated and the F DO₂ measured on the bench. Indiscriminate use of prediction formulas exposes the practitioner to errors in O₂ administration assessment. Our study proposed a new prediction formula that takes into account minute ventilation and the ratio of the inspiratory time to the total breathing cycle time during oxygen delivery via a heat-and-moisture exchanger.

Model and Settings. Spontaneous breathing was generated in ambient temperature and barometric pressure conditions with a mechanical test lung (Model 5600i Dual Test Lung, Michigan Instruments, Grand Rapids, Michigan), which included 2 independent artificial lungs. With a special lung coupling clip, one lung was used to drive the second lung to achieve spontaneous breathing simulation. The settings of the artificial lung were as follows: resistance: 5 cm H₂O/L/s and compliance of 0.06 L/cm H₂O. The first lung was driven by a mechanical ventilator, Servo-i (Maquet, Getinge group, Getinge, Sweden), set to volume control mode (continuous flow without auto-flow, time pause, and an inspiratory rise time at 0%; PEEP of 0 cm H₂O; the trigger was set at −10 cm H₂O to avoid self-triggering). The O₂ flow from a wall-mounted Thorpe Tube (0 to 15 L/min; Air Liquide RTM3, Technologie medicale, Noisy Le Sec, France) was delivered through an HME filter (dead space volume: 16 mL; Tracheolife I Filter HME Kendall-Covidien, 353U19004, Medtronic, Dublin, Ireland). The HME filter was directly fixed to a flow sensor. The flow sensor was directly connected to the entry of the lung port inlet of the second Dual Test Lung (Fig. 1). An O₂ analyzer port was located on the top plate of the second artificial lung. The 3 parameters were modified as followed:

1. O₂ flow: 2, 3, 4, 5, 6 L/min.
2. V̇E: 5, 10, 15, 20 L/min.
3. T_I/T_{tot}: 0.33 and 0.50.

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Supplementary material related to this paper is available at http://www.rcjournal.com.

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Note: With these $V_E$ and $T_I/T_{tot}$ values, $V_I$ ranges from 10 to 60 L/min (Table 1).

**Variables.** The main measured variable was $F_DO_2$, expressed as the volumetric percentage of $O_2$ in the steady-state dual test lung. $F_DO_2$ was measured with a Datex Ohmeda $O_2$ Monitor (Model 5120, Louisville, Kentucky) calibrated with room air (21%), then at 30%, 35%, and 50%, with certified $O_2$ gas (sensor type, galvanic fuel cell reference 0237–2034 –700; accuracy, ±2% of full scale; response time, 9 s; measuring range, 0–100%). $F_DO_2$ was measured as the mean of 15 breaths after a stabilization period of at least 1 min.

$O_2$ flow was measured continuously with a Thermal $O_2$ Mass Flow Meter (Red Y Vögtlin Instruments, Switzerland, Aesch) (accuracy, ±1.5% of full scale; repeatability, ±0.1% of full scale). The $V_E$ and $T_I/T_{tot}$ were measured with a data acquisition system IX-214 (iWorx Systems, New Hampshire), which included an SP-304 (iWorx Systems, New Hampshire) flow sensor and a data-acquisition hardware connected to a Software Labscribe 3 (Iworx).

The flow sensor was calibrated by using a 1-L calibration syringe (Hans Rudolph, Inc., Shawnee, Kansas) and ambient air. During this step, the gap between the required value and read value was a maximum of ±30 mL. All measurements were done in triplicate.

### Part 2

The calculated $F_DO_2$ values were compared with the $F_DO_2$ values obtained through the following 2 previously validated formulas:

- **The Shapiro formula,**

  \[
  F_{DO_2} = 0.20 + (0.04 \times L/min O_2)
  \]

- **The Vincent formula,**

  \[
  F_{DO_2} = 0.21 + (0.03 \times L/min O_2)
  \]

### Statistical Analysis

Data were analyzed by using the Sigma plot software (Version 12.0 Systat Software Inc., San Jose, California).
The values are expressed as mean ± SD. The agreement between F_DO2 calculated by the mathematical model and the F_DO2 measured during the bench test measurements was expressed as proposed by Bland and Altman. As such, the bias and the limits of agreement were reported for each TI/Ttot (95% CI for the difference between measurements). An intraclass correlation coefficient was calculated to measure the relationship between F_DO2 calculated and F_DO2 measured for each TI/Ttot. To analyze the variability between the F_DO2 calculated with our formula and the FDO2 measured, a coefficient of variation was calculated for each TI/Ttot. Finally, an agreement between F_DO2 calculated by using the prediction formulas (Shapiro and Vincent), and the FDO2 measured during the bench test measurements was calculated.

Results

In this bench study, when the O2 flow and/or the TI/Ttot increased, the F_DO2 increased. When the V_E increased, the F_DO2 decreased (Fig. 2).

Part 1

The results of the Bland-Altman method between F_DO2 calculated by using our mathematical model and the FDO2 measured showed that the bias value was 1.49 ± 0.84%, and the limits of agreement ranged from −0.17% to 3.14% (Fig. 3). The intraclass correlation coefficient results were 0.991 for TI/Ttot = 0.33 and 0.994 for TI/Ttot = 0.50, and the coefficient of variations were 2.1% for TI/Ttot = 0.33 and 1.3% for TI/Ttot = 0.50 (Fig. 3).

Part 2

The results of the Bland-Altman method for the F_DO2 calculated by the Shapiro formula and the FDO2 measured on the bench showed that the bias value was 0.075 ± 8.66%, and the limits of agreement ranged from 16.89% to 19.84% (Fig. 4). For the Vincent formula, the bias value was 3.08 ± 8.56% and the limits of agreement ranged from −13.69% to 19.84% (Fig. 4).

Discussion

During O2 administration through an HME in patients with tracheostomy and who breathed spontaneously, slight absolute differences were found between the F_DO2 calculated with our formula and the FDO2 measured on the bench. The bias (with its limits of agreement), the intraclass correlation coefficient, and the coefficient of variation were...
underestimation of oxygenation. The $V_\dot{I}$ value is equal to

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in adult patients, because the $V_\dot{I}$ value was much higher

from 5 to 20 L/min), and the ratio of the inspiratory time ($T_I$) to the
total breathing cycle time ($T_{tot}$) ($T_I/T_{tot}$) of 0.33 ($T_I/T_{tot}$ value) and
0.50 ($T_I/T_{tot}$ value). Inspiratory flow ($V_\dot{I}$) that ranged from 10 to
60 L/min. The center line denotes mean, dashed lines show ±1.96
SD.

Fig. 3. Bland-Altman graph comparing the fraction of delivered O2
(FDO$_2$) calculated with our formula and the FDO$_2$ measured on the
bench for an O$_2$ flow of 2–6 L/min, a minute ventilation that ranged
from 5 to 20 L/min, and the ratio of the inspiratory time ($T_I$) to the
total breathing cycle time ($T_{tot}$) ($T_I/T_{tot}$) of 0.33 ($T_I/T_{tot}$ value) and
0.50 ($T_I/T_{tot}$ value). Inspiratory flow ($V_\dot{I}$) that ranged from 10 to
60 L/min. The center line denotes mean, dashed lines show ±1.96
SD.

low between the FDO$_2$ measured and the FDO$_2$ calculated,
which indicated the suitable validity of our prediction formul.
However, when the FDO$_2$ increased, this bias varied,
in an inversely proportional manner, and was probably due
to the turbulence during high O$_2$ flow.23 Bias between the
FDO$_2$ calculated and the FDO$_2$ measured of both prediction
formulas (Shapiro and Vincent) were small and showed
slight differences (bias for the Shapiro formula, 0.075 ±
8.66%; and for the Vincent formula, 3.08 ± 8.56%). How-
ever, the SD of these biases and the limits of agreement
were wider compared with the values obtained with our
formula.

According to our calculations, both prediction formulas
were well suited for a healthy adult patient breathing at
rest ($V_\dot{E} =$ ±8 L/min and $T_I/T_{tot}$ = 0.33). This meant that
these formula minute volumes were less suitable when the
$V_\dot{E}$ values differed from this threshold. Therefore, the Shap-
rio and the Vincent formulas should be used cautiously.
Indeed, not considering these facts could lead to an over-or
underestimation of oxygenation. The $V_1$ value is equal to
the ratio between the minute volume and the $T_I/T_{tot}$ ($V_1$ =
$[f \times V]/[T_I/T_{tot}]$). According to our formula, the FDO$_2$ was
roughly equal to the ratio between the O$_2$ flow and $V_1$. So,
in adult patients, because the $V_1$ value was much higher
than the O$_2$ flow value, the impact of $V_1$ on FDO$_2$ was
higher. However, in small patients, it was the opposite: the
O$_2$ flow was higher than the $V_1$. In this case, small varia-
tions of O$_2$ flow will have a major impact on FDO$_2$. Ac-
cording to our research, this variation appears in several
studies.1,10,11,19,22 Thus, for instance, when taking into con-
sideration two $V_1$ values, the gap between both FDO$_2$ val-
ues increases when the O$_2$ flow increases (Fig. 2). Con-
sequently, during O$_2$ therapy, if the ventilatory pattern was
not constant, then the FDO$_2$ would not be constant either.
When the O$_2$ flow is constant:

- If the $V_1$ increases, then the FDO$_2$ will decrease. For ex-
ample, under conditions of stress, hyperthermia, agita-
tion, metabolic acidosis, pain, or exercise (eg, COPD
rehabilitation).1,23 Similar observations were found by
Couser and Make12 with subjects oxygenated through a
transtracheal catheter. These investigators observed that
a decrease in $V_1$ increased $P_{aO_2}$.

- If the $V_1$ decreases, then the FDO$_2$ will increase. For
example, under some sedative medications and/or in-
stances of drug abuse, as well as in reassuring and re-
 laxing atmospheres, or when patients are in a deep sleep
and are receiving O$_2$ by low flow.11,15,24

- If the $V_1$ is small, then the FDO$_2$ value will be high, even
with low O$_2$ flow (eg, during O$_2$ therapy in preterm
infants).

These situations should encourage us to be cautious
when $V_1$ varies during oxygenation at low flow because
this can lead to a risk of over or under oxygenation. In-
 deed, if hypoxemia (or hyperoxemia) is only due to ven-
tilatory pattern variations, it is enough to modify the O$_2$
flow to adjust the value of arterial pressure in O$_2$. There
are other considerations with regard to the dead space of
the HME. Indeed, first, during spontaneous ventilation with
HMEs, the mixture with expired air could affect the O$_2$
fraction of inspired air. However, the dead-space value of
these devices generally varies from 9 to 29 mL25 and was
16 mL in the HME used in our study.

Second, a tracheostomy tube reduces the upper-airway
anatomic dead space by up to 150 mL, or 50%.26 In these
cases, the CO$_2$ contained in the anatomic dead space
is lower than in normal physiologic ventilation. Therefore,
the impact on the FDO$_2$ decrease would be limited. Third,
during oxygenation with an O$_2$ administration device, dur-
ing the expiratory phase, the continuous O$_2$ flow washout
reduces the dead space, which limits the impact of CO$_2$
rebreathing.14 The clinical utility of knowing the formula
is that it could be helpful for the therapist to be aware of
the initial setup for O$_2$ therapy for specific situations. For
example, for small patients (or lower $V_1$), low O$_2$ flow can
deliver high FIO$_2$, for tall people (or high $V_1$), high O$_2$ flow
delivers less FIO$_2$ than with normal $V_1$, and during high O$_2$
flow in adults, any variation of $V_1$ will change the FIO$_2$
dramatically.
The aim of this bench study was to validate a new formula to predict F$_{DO2}$ during oxygenation through an HME. The V˙E and the analyzed O$_2$ flow ranged from 5 to 20 L/min (Table 1) and from 2 to 6 L/min, respectively. However, we draw attention to the risk of under humidification of inspired gas during high O$_2$ flow through an HME in patients who are able to breathe spontaneously.25

Study Limitations

The present study had some limitations. In practice, use of our prediction formula was difficult because the exact patient V˙I value was unknown and O$_2$ flow meters have a low accuracy.27-29 Moreover, in this study, the V˙I used was continuous (rectangular form). However, the human V˙I wave is not continuous (waveform). As such, determining the exact value of F$_{DO2}$ is difficult in clinical situations. In addition, our model had limitations because it did not reproduce anatomic dead space. Also, the HME used was Tracheolife I, other systems exist with different dead spaces, which could affect results.

Conclusions

During supplemental oxygenation at low flow in a model of spontaneous breathing with an artificial airway, the F$_{DO2}$ was influenced by the O$_2$ flow and the V˙I. According to our observations, the V˙I had a substantial impact on the F$_{DO2}$ and, therefore, could lead to over or under oxygenation without careful monitoring. F$_{DO2}$ comparisons between the prediction formulas typically used by clinicians and F$_{DO2}$ measured on the bench had larger differences.

Caution should be exercised when using these formulas for predicting F$_{DO2}$. Indeed, during the calculation of the P$_{aO2}$/F$_{IO2}$ with the Shapiro or Vincent formulas, there was a high risk of overestimating the F$_{IO2}$, especially if the patient’s inspiratory rate was high. This paper proposed a new prediction formula that takes into account O$_2$ flow and V˙I values. Our prediction formula showed good accuracy when predicting F$_{DO2}$ during supplemental oxygenation at low flow through an HME.

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