

Reliability of Airway Occlusion Pressure as an Index of Respiratory Motor Output

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BACKGROUND: Airway occlusion pressure 0.1 s after the start of inspiratory flow ($P_{0.1}$) is used as an index of respiratory motor output; however, the reliability of $P_{0.1}$ in this capacity has not been sufficiently investigated. Therefore, the aim of our study was to examine the reliability of $P_{0.1}$. **METHODS:** Eleven healthy subjects (7 men and 4 women) participated in our study. Subjects were placed in a supine position, and $P_{0.1}$ was measured every 30 s for 5 min, following a 1-min period during which ventilation and breathing frequency were measured. A total of 10 $P_{0.1}$ values were obtained, and the intraclass correlation coefficient (ICC) was used to analyze reliability. ICC values from ICC (1, 2) to ICC (1, 10) were calculated following a number of measurements (k), where ICC (1, k) was increased sequentially from 2 to 10. **RESULTS:** The ICC (1, 2) through ICC (1, 10) values were found to be between 0.877 and 0.960 (95% CI 0.565–0.966 and 0.912–0.987, respectively). When the target coefficient was set at 0.9, the ICC (1, 1) from 10 measurements was calculated a minimum of 4 times. **CONCLUSIONS:** Although a single measurement of $P_{0.1}$ was somewhat reliable, the 95% CIs indicated that it is necessary to determine the average value of 3 or more measurements. The minimum of 4 repeat measurements were required to obtain valid results, indicating that the current method of determining $P_{0.1}$ by averaging the values from at least 4 repeated measurements is valid. *Key words:* airway occlusion pressure; respiratory motor output; intraclass correlation coefficient; airway occlusion system; measurement validity. [Respir Care 2013; 58(5):845–849. © 2013 Daedalus Enterprises]

Introduction

The measurement of respiratory motor output is important for assessing respiratory diseases. While respiratory motor output is predominantly evaluated by measuring phrenic nerve activity or through electromyography (EMG), the measurement of respiratory muscle activity using surface electrodes is very difficult, particularly in the diaphragm. Although it is not possible to measure the activity of the phrenic nerve by invasive in vivo methods, diaphragm activity may be measured by surface EMG in the

regions of the fifth, sixth, and seventh intercostal spaces, via the rib cage.¹ However, as the intercostal and abdominal muscles are also localized around the diaphragm, these measurements can be complicated by cross-talk. Although other methods, such as the direct use of an esophageal electrode, inserted needle, or wire electrodes, are able to measure diaphragm EMG, these methods are invasive.^{2,3} An alternative to measuring respiratory motor output is to measure the airway occlusion pressure 0.1 s after the start of inspiratory flow ($P_{0.1}$), using an airway occlusion system.⁴⁻⁷ The $P_{0.1}$ is both measurable and useful in the assessment of a number of variables, such as the respiratory motor output in various diseases,⁸⁻¹² the criterion of weaning,^{13,14} effective respiratory impedance,^{15,16} and the non-invasive tension-time index.¹⁷

Ventilatory drive is classically measured by the breathing frequency and minute ventilation (\dot{V}_E) for assessment of conditions such as exercise hypoxia and/or hypercapnia. The tidal volume (V_T) and inspiratory time, which is a timing factor of breathing frequencies, can also be used to calculate the duty cycle index of respiratory center

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output (V_T /inspiratory time).¹⁸ However, V_T and inspiratory time are not always sufficient for the evaluation of respiratory center output, because they are affected not only by the mechanical properties of the lung and chest wall, but also by airway resistance.⁶ In contrast, the $P_{0.1}$ is not affected by either of these factors because it is not dependent upon air flow, and the lung elastic pressure is equal to the chest-expanding pressure at functional residual capacity (FRC). Therefore, as $P_{0.1}$ is much less affected by the mechanical properties of the lung and chest wall, in comparison with V_T and breathing frequency, it is superior to other indices of respiratory motor output.

The average value of $P_{0.1}$ is generally calculated from several independent measurements in order to correct for variations due to respiratory flicker and measurement errors.¹⁹⁻²² However, the reliability of the $P_{0.1}$ value in the evaluation of respiratory motor output and the number of measurements required to ensure its validity have not been sufficiently investigated. The coefficient of variation is often used for confirming the reliability of measurements, but this method expresses only extent of variation of the values. The intraclass correlation coefficient (ICC)²³⁻²⁵ is more useful than the coefficient of variation, because it directly reflects the reliability and helps determine the minimum number of repeated measurements. The purpose of our study was to statistically evaluate the reliability and validity of $P_{0.1}$ measurements using the ICC.

Methods

Subjects

Eleven healthy students, free of cerebrovascular, respiratory, and cardiovascular diseases, participated in our study (7 men and 4 women, age 20.8 ± 0.4 y, height 163.5 ± 10.1 cm, body weight 60.2 ± 12.0 kg). While the outline of our study was explained to all subjects, and written informed consent was obtained, the true aim of the study was hidden until the completion of all procedures. This study was approved by the ethics committee of Nihon Institute of Medical Science (10-009).

Measurement of Airway Occlusion Pressure

An airway occlusion system (model 9326, Hans Rudolph, Shawnee, Kansas, dead space 48.9 mL), assembled from a T-type 2-way rebreathing valve and an inflatable balloon-type airway occlusion system, was used to measure $P_{0.1}$ by manual manipulation.

The time from the initiation of the switch operation until the balloon completely occluded the inspiration port was < 100 ms. A differential pressure transducer (TP-602G, Nihon Koden, Tokyo, Japan) was connected to the side port of the airway occlusion system via a 4-mm-wide tube,

QUICK LOOK

Current knowledge

Airway-occlusion pressure 0.1 s after the start of inspiratory flow ($P_{0.1}$) is useful in assessing respiratory motor output, the risk of extubation failure, the effective respiratory impedance, and the noninvasive tension-time index. $P_{0.1}$ is measured 3 or 4 times, and the mean $P_{0.1}$ is reported.

What this paper contributes to our knowledge

The minimum number of $P_{0.1}$ measurements required for a valid $P_{0.1}$ was 4. All the $P_{0.1}$ measurements must be taken under the same conditions.

to measure mouth pressure, while a hot-wire flow transducer of the gas analyzer (AE-300S, Minato Medical Science, Osaka, Japan) was connected to the expiratory port. A mouth mask (MAS0215, Minato Medical Science, Osaka, Japan) was also connected to the mouth port of the airway occlusion system. The breathing frequency, V_T , \dot{V}_E , and end-tidal carbon dioxide (%) were measured with each breath. The analog signal from the gas analyzer, as well as signals measuring the switch of the balloon shutter and differential pressure transducer, were continuously recorded at 1,000 Hz via an analog-to-digital converter (PowerLab, ADInstruments, Sydney, Australia), and the data were analyzed using waveform analysis software (Chart 5.3, ADInstruments, Sydney, Australia).

Procedure

All experiments were performed in a quiet room. Subjects lay in the supine position, and the mouth mask was attached and held in place using straps. To prevent the subjects from predicting measurements, they were provided with headphones to silence mechanical operation sounds. Subjects breathed calmly for 6 min. After 1 min, $P_{0.1}$ values were measured every 30 seconds for the 5 min following the initial measurement. All measurements were performed by a single operator experienced with the airway occlusion device.

Data Analysis

Inspiration was obstructed using a balloon occlusion system, in which the balloon was inflated slightly before the end of expiration, and deflated immediately after a negative change in airway pressure was detected. The $P_{0.1}$ value was recorded 100 ms after the onset of inspiration. When the airway pressure was negative at the time of switch operation, it was

judged that airway occlusion occurred during inspiration, and the values were excluded from analysis. The time from switch operation to the initiation of inspiration was calculated using the switch signal and waveform of airway pressure, and the essential airway occlusion time was calculated from the onset of inspiration to the time at which the balloon deflated and airway pressure returned to normal. All $P_{0.1}$ values are expressed as absolute values.

Statistical Analysis

In order to analyze the influence of $P_{0.1}$ measurement on respiration, the breathing frequency, V_T , \dot{V}_E , and end-tidal carbon dioxide values obtained during the first minute of the experiment, during which $P_{0.1}$ was not measured, were compared to those obtained during the last minute of the experiment, during which $P_{0.1}$ was measured concurrently. The reliability of the $P_{0.1}$ values was assessed using the coefficient of variation and the ICC. Intra-rater reliability [ICC (1, 1) = ρ_1] was calculated from 10 sequential $P_{0.1}$ values. Obviously erroneous values were excluded from these calculations. Generally, it is possible to decrease variance due to accidental error by determining the mean value of repeated measurements. To calculate the minimum number of repetitions required to obtain valid results, the number of measurements (k) was increased sequentially from 2 to 10, and the resulting ICC (1, 2) through ICC (1, 10) values were calculated. The between-target mean square and within-target mean square values were calculated from the results of 1-way analysis of variance. The standard error of mean (SEM) was calculated using the following formula:

$$SEM = \sqrt{(BMS - WMS)k \times (1 - \rho_1)} \quad (1)$$

where BMS is the between-target mean square, and WMS is the within-target mean square. The minimum number of repetitions required for valid results was calculated using the following formula, where the target coefficient value $\rho_2 = 0.9$:

$$\text{Minimum number of repetitions (k)} = \rho_2 \times (1 - \rho_1) / \rho_1 \times (1 - \rho_2)$$

We used statistics software (SPSS 13.0, SPSS, Chicago, Illinois) for all statistical analyses. Statistical significance was indicated when $P < .05$.

Results

The average time from the onset of balloon inflation to the onset of inspiration was 563 ± 258 ms, while the essential airway occlusion time was 401 ± 84 ms. The

Table 1. Respiratory Variables Before and During $P_{0.1}$ Measurement

	Before mean \pm SD	During mean \pm SD	<i>P</i>
f, breaths/min	16.4 \pm 3.9	16.3 \pm 4.3	.91
V_T , L	0.7 \pm 0.1	0.6 \pm 0.1	.13
\dot{V}_E , L/min	10.7 \pm 2.4	9.8 \pm 2.9	.10
End-tidal carbon dioxide, %	5.4 \pm 0.5	5.3 \pm 0.4	.34

$P_{0.1}$ = airway-occlusion pressure 0.1 s after the start of inspiratory flow
 f = breathing frequency
 V_T = tidal volume
 \dot{V}_E = minute ventilation

Table 2. $P_{0.1}$ Results

Subject	$P_{0.1}$ (cm H ₂ O) mean \pm SD	Coefficient of Variation (%)
1	1.41 \pm 0.53	37.6
2	0.88 \pm 0.34	38.7
3	4.83 \pm 1.81	37.5
4	0.65 \pm 0.11	16.6
5	1.72 \pm 0.85	49.6
6	0.67 \pm 0.34	50.7
7	1.12 \pm 0.22	20.0
8	2.01 \pm 0.58	28.8
9	2.17 \pm 0.62	28.7
10	1.31 \pm 0.48	36.9
11	0.82 \pm 0.34	41.1

$P_{0.1}$ = airway-occlusion pressure 0.1 s after the start of inspiratory flow

breathing frequency, V_T , \dot{V}_E , and end-tidal carbon dioxide values measured during the first and last minutes of the experiment were not significantly different (Table 1). The average $P_{0.1}$ values of the 11 subjects examined in this study were 0.65–4.82 cm H₂O, while the average coefficient of variation values were 16.6–50.7% (Table 2). The $P_{0.1}$ value for 10 measurements were ICC (1, 1) = 0.704 (95% CI 0.509–0.885), and ICC (1, 2) through ICC (1, 10) = 0.877–0.975 (95% CI 0.565–0.992, SEM 0.48–0.65) (Table 3). When the target coefficient value was set at 0.9, it was found that a minimum number of 3.8 measurements were required for a valid result to be calculated, as indicated by the ICC (1, 1) value.

Discussion

V_T and breathing frequency values are conventionally used as indices of respiratory motor output, because they include the entire respiratory system.¹⁸ However, it is desirable to exclude effects due to mechanical properties, such as compliance of the lung and chest wall and airway resistance. It is difficult to uniformly estimate respiratory motor output using the breathing frequency and/or V_T

Table 3. Change of ICC When the Number of Measurements Was Increased Sequentially

ICC (1, k)	Estimated ICC	95% CI	SEM
1, 2	0.877	0.565–0.966	0.63
1, 3	0.940	0.837–0.982	0.57
1, 4	0.956	0.892–0.987	0.54
1, 5	0.973	0.937–0.992	0.48
1, 6	0.975	0.942–0.992	0.54
1, 7	0.967	0.926–0.990	0.60
1, 8	0.952	0.894–0.985	0.65
1, 9	0.961	0.913–0.988	0.64
1, 10	0.960	0.912–0.987	0.63

ICC = intraclass correlation coefficient

k = number of measurements

SEM = standard error of the mean

values when airway resistance increases, or when the volume-pressure diagram, which signifies the relationship between lung volume and pressure produced by the respiratory system, changes. For example, breathing frequency and \dot{V}_E are increased in patients with emphysema or cystic fibrosis, in comparison with healthy subjects, although there is no difference in V_T .^{26–28} In contrast, the $P_{0.1}$ is not affected by the compliance of the lung and chest wall, due to the measurement of FRC, or by airway resistance, due to the measurements of airway pressure being taken in the absence of air flow. Therefore, $P_{0.1}$ has been widely used as an alternative value for respiratory motor output.

It is also possible to facilitate ventilation by measuring the $P_{0.1}$ when the airway is occluded for approximately 0.5 seconds. However, the occlusion procedure is not presumed to affect the respiratory control system via the vagal reflex, and many previous studies have used occlusion systems that open the airway semi-automatically within 120–150 ms from the onset of inspiration.^{19–21} Investigators have also used manual manipulation to open this system approximately 400 ms after the onset of inspiration.²² The average duration of occlusion in our study was also approximately 400 ms; however, as the V_T and breathing frequency before measuring the $P_{0.1}$ were not significantly different from those obtained during the measurement of $P_{0.1}$, we do not believe that this occlusion affected ventilation.

The use of $P_{0.1}$ as an index of respiratory motor output has been investigated due to some concern about the validity of this measurement. Eldridge has reported that the intratracheal pressure during airway occlusion is linearly related to the phrenic electrical activity in animal experiments, which is considered to be direct evidence of respiratory motor output.²⁹ Lopata et al compared phrenic nerve activity and intratracheal pressure in intact cats, and further demonstrated that diaphragmatic activity is related to

airway occlusion pressure in healthy subjects at 150 ms after the onset of inspiration.³⁰ These findings, as well as the relationship between $P_{0.1}$ and other ventilatory parameters, provide evidence for the validity of $P_{0.1}$ as an index of respiratory motor output.^{30–33} However, it has been suggested that to obtain the most accurate results the respiratory system should remain under the same conditions, such as the same lung volume and posture, when $P_{0.1}$ is measured.¹ For example, a study of electrical phrenic nerve stimulation found that increasing FRC decreased the transdiaphragmatic pressure generated in response to a given electrical stimulus.³⁴ Diaphragmatic activity is also absent during the measurement of $P_{0.1}$ at lung volumes lower than FRC, because inspiration occurs through elastic expansion pressure of the chest wall at these low lung volumes. Although the activity of expiratory muscles, such as the transverse abdominal and oblique muscles, increases to exhale air below FRC, this in itself does not contradict the importance of $P_{0.1}$ as a comprehensive indication of respiratory motor output. Moreover, measuring diaphragm EMG provides only an evaluation of inspiratory muscles, while $P_{0.1}$ evaluates the activity of all motor output to respiratory muscles, including both inspiratory and expiratory muscles. Consequently, $P_{0.1}$ measurements are considered a good index for the evaluation of respiratory motor output.^{21,22}

It is common to average the values of a number of measurements of breathing frequency and V_T taken over a period of 30 seconds to a few minutes, because of the variability of these measurements. Although the $P_{0.1}$ is temporal, it is highly probable that it is related to breathing frequency and V_T , and the determination of a representative average value obtained from several measurements is therefore also necessary. However, the number of measurements used by various researchers has varied (for instance, Grassino et al used 10 measurements,²² Ramonatxo et al used 4,^{20,21} and Whitelaw et al used 12⁵), and to date, no study has investigated the minimum number of measurements required to obtain valid $P_{0.1}$ values. Although to some extent a single $P_{0.1}$ measurement was found to have good reliability in our study, the ICC (1, 1) was 0.704 (95% CI 0.509–0.885). Therefore, when the 95% CI was considered, it was necessary for an average of at least 3 measurements to be calculated (95% CI of ICC (1, 3) 0.837–0.982). As the lower confidence limit is sufficiently larger than 0.8 and constant when 4 or more measurements are included, we consider the use of 4 measurements to result in a valid $P_{0.1}$ value.

Since the length of the diaphragm is short when the lung volume increases, the contractile force of the diaphragm at higher lung volume decreases³⁴ even if the respiratory motor output does not change.⁶ In the upright position (compared with supine position), increasing the FRC may result in a decrease in the $P_{0.1}$ value, with no change in respiratory motor output. The breathing frequency in the

upright position is larger than in the sitting position because of increased O_2 consumption. Those differences may affect the stability of the measurement of $P_{0.1}$. Furthermore, respiratory motor output is not constant in abnormal breathing patterns such as Cheyne-Stokes respiration. In this condition, measurement of $P_{0.1}$ may require more repetitions than the minimum number calculated in our study. Thus, it is necessary to consider the reliability of the measurement of $P_{0.1}$ in each position and in various diseases.

Conclusions

In this study we have demonstrated that the minimum number of repeat measurements required for the calculation of a valid $P_{0.1}$ value is 4. Furthermore, when determining $P_{0.1}$, all experimental measurements must be taken under common conditions. We therefore suggest that an average $P_{0.1}$ value be calculated from a minimum of 4 measurements in order to obtain valid and reliable results.

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