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Assessment of the Hypercapnic Ventilatory Response Measured with the Transcutaneous and Inspired Partial Pressures of CO_2

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ABSTRACT

Purpose : The slope of the hypercapnic ventilatory response (HCVR) can be calculated from the values of transcutaneous partial pressure of CO_2 ($tcPCO_2$) and inspired partial pressure of CO_2 (P_ICO_2) without measuring ventilatory volume. In this study, we examined how accurately this calculation reflects the slope derived directly from measured expiratory volume (V_E).

Methods : We assessed hypercapnic ventilatory responses in 3 men, and measured HCVR with both methods 4 times in each.

Results : We found a significant correlation between the slope calculated from $tcPCO_2$ and P_ICO_2 and the slope derived directly from measured HCVR.

Conclusion : We conclude that use of $tcPCO_2$ and P_ICO_2 is a valid method for estimating HCVR. (Jikeikai Med J 2005 ; 52 : 59-62)

Key words : hypercapnic ventilatory response, CO_2 electrodes, transcutaneous

INTRODUCTION

Measuring hypercapnic ventilatory response (HCVR) in neonates is extremely difficult, because alveolar ventilatory volume cannot be measured easily. Alveolar ventilatory volume is calculated from the exhaled volume of CO_2 during breathing ($\dot{V}co_2$) and the fractional concentration of alveolar CO_2 (F_ACO_2) according to the following formula :

$$\dot{V}_{A(\text{breathing air})} = \dot{V}co_2 / F_Aco_2 \qquad [\text{Eq } 1]$$

If the fractional concentration of CO_2 in inspired gas (F_Ico_2) is added, the formula is as follows :

$$\dot{V}_{A(\text{breathing } CO_2 \text{ in air})} = \dot{V}co_2 / (F_Aco_2 - F_Ico_2) \qquad [\text{Eq } 2]$$

The fractional increase in ventilation from breathing air to breathing air/CO_2 (VR : ventilatory ratio) is :

$$VR = \frac{\dot{V}_A \text{ (breathing } CO_2 \text{ in air)}}{\dot{V}_A \text{ (breathing air)}} = \frac{F_Aco_2}{F_Aco_2 - F_Ico_2} \qquad [\text{Eq } 3]$$

Hazinski et al.[1] obtained the following equation by replacing F_ACO_2 with transcutaneous partial pressure of CO_2 ($tcPCO_2$), which shows VR when the inspired partial pressure of CO_2 (P_ICO_2) is added :

$$VR = \frac{tcPco_2 \text{ (breathing air)}}{tcPco_2 - P_Ico_2 \text{ (breathing } CO_2 \text{ in air)}} \qquad [\text{Eq } 4]$$

VR is a value that is expressed as the ratio of ventilatory volume change when the ventilatory volume at a steady state during air breathing is defined as 1. The increase in VR against the changes in

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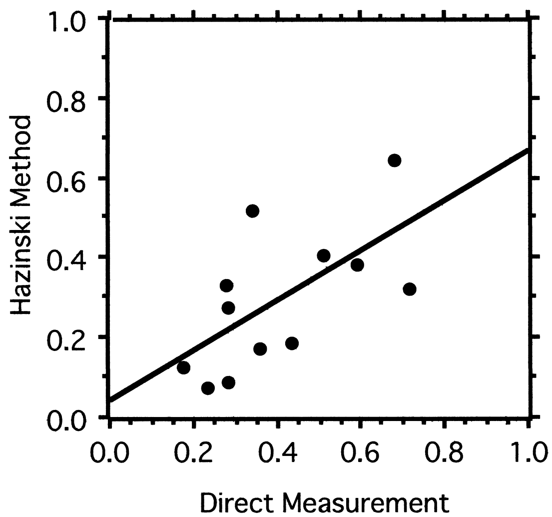

Fig. 1. The regression line between the slopes of the HCVR measured with the Hazinski method, which measures $tcPco_2$, and with direct measurement of minute ventilation was $Y=0.041+0.627 \cdot X$. The two slopes were strongly correlated. ($R^2=0.404$, $P=0.026$; $n=12$).

$tcPCO_2$ is the slope S of HCVR: S=VR/(T2−T1), where T2 and T1 are the $tcPCO_2$ values with and without added CO_2. For example, the normal HCVR is about 3 L/min/mmHg. With an assumed resting ventilation of 6 L/min, the slope S with the Hazinski method is 3/6=0.5/mmHg[2].

Thus, they calculated the slope of HCVR from the values of $tcPCO_2$ and P_ICO_2 without measuring alveolar ventilatory volume.

It is not known how accurately the slope that is calculated from $tcPCO_2$ reflects the slope that is based on directly measured expiratory volume (V_E), a standard indicator of HCVR. We therefore performed a study to assess the accuracy of calculating the slope from $tcPCO_2$ and P_ICO_2 (the Hazinski method) by comparing it with the slope derived from direct measurement of V_E.

Materials and Methods

The protocol was approved by the ethics committee of The Jikei University School of Medicine, and informed consent was obtained from each subject. The subjects were 3 healthy men. Age, height, and weight were 40 years, 176 cm, and 78 kg, respectively, in subject a; 41 years, 161 cm, and 79 kg in subject b; and 51 years, 167 cm, and 63 kg in subject c. The HCVR was determined with both the Hazinski method[1] and direct measurement of V_E. The VR was measured 4 times with each method in each of the 3 subjects. The subjects breathed room air and oxygen or a mixture of oxygen and exhaled gas through a one-way valve attached to a face mask in a semisitting position (Fowler's position). The tip of the sampling tube was placed close to the mouth and end-tidal CO_2 pressure and P_ICO_2 were measured with a capnometer (Capnomac Ultima Expiratory Gas Analyzer; Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland). The capnometer was calibrated with dry gas and compensated for barometric pressure and vapor pressure. Minute ventilation was measured with a hot-wire spirometer (Respiratory Flowmeter; Minato Medical Science Co., Ltd., Osaka, Japan), placed between the face mask and the respiratory circuit. The details of the experimental set up described in Fujiwara et al.[3].

Inspiratory oxygen concentration was kept higher than 50% throughout the experiment. After the skin electrode (TCM3; Radiometer A/S, Bronsho, Denmark) was placed on the internal side of the forearm, the face mask was attached, a mixture of air and oxygen was inhaled, and $tcPCO_2$ and V_E were measured as steady state values. The inspired CO_2 was then increased in two steps of 3 to 5 mmHg each; stabilized P_ICO_2, $tcPCO_2$, and V_E were recorded at each step. Minute ventilation was calculated from each tidal volume and was traced on the chart recorder to confirm that the value was stable for 1 minute.

For the Hazinski method, VR was calculated (Eq 4) for each HCVR test at a steady state and at the first and second steps of CO_2 loading. From these three sets of VR data and the $tcPCO_2$ data, the slopes of the regression lines were obtained.

For directly measured minute ventilation, measured minute ventilation was divided by steady state minute ventilation to obtain VR. From these three sets of VR data and the $tcPCO_2$ data, slopes of the regression lines were obtained.

Data are expressed as mean±SE. Differences with a P value less than 0.05 were considered statistically significant. The StatView software package (Abacus Concepts, Berkeley, CA) was used for regression analysis.

Results

With the Hazinski method, the value of the slopes of the regression lines for HCVR obtained from 4 measurements in each of the 3 subjects was 0.30 ± 0.05/ mmHg ($n=12$; Table 1). For directly measured minute ventilation, the value of the slopes of the regression lines for HCVR obtained from 4 measurements in each of the 3 subjects was 0.41 ± 0.05/mmHg ($n=12$; Table 1). The slopes obtained with these two methods were significantly correlated ($R^2=0.404$, $P=0.026$; $n=12$).

Table 1. Slopes of the hypercapnic ventilatory response obtained with the Hazinski method and with direct measurement of minute ventilation

Subject	Test	Slope: Hazinski Method	Slope: Direct Measurement
Subject a	1	0.330	0.275
	2	0.521	0.339
	3	0.088	0.282
	4	0.407	0.507
Subject b	1	0.175	0.358
	2	0.073	0.230
	3	0.275	0.282
	4	0.124	0.174
Subject c	1	0.189	0.434
	2	0.385	0.588
	3	0.644	0.678
	4	0.323	0.715

Discussion

This study shows that the slope of HCVR calculated from the values of transcutaneous PCO_2 is correlated well to the directly measured HCVR.

When HCVR is directly measured in healthy subjects without hypercapnia, the increase in ventilation per 1 mmHg of arterial partial pressure of CO_2 ($PaCO_2$) is 50% of the steady state ventilation. For example, when minute ventilation is 6 L/min, ventilation increases by 3 L/min, and the slope is 3 L/min/mmHg of $PaCO_2$. If we convert these numbers to reflect the ventilatory response that Hazinski et al.[1] found based on $tcPCO_2$ in newborns, ventilation would have increased from 1 to 1.5 L/min and the slope would be 0.5 L/min/mmHg of $PaCO_2$[2]. In our study the slope calculated from direct measurement of minute ventilation was 0.41 ± 0.05 ($n=12$), which is close to the expected value.

However, the slope we calculated on the basis of $tcPCO_2$ was 0.30 ± 0.05 ($n=12$). How can this low value be explained? The $tcPCO_2$ is thought to reflect $PaCO_2$ accurately[4], and there would be no significant error in measuring ventilation. However, with the Hazinski method, CO_2 clearance is estimated with alveolar ventilation, not with total ventilation. Therefore, changes in dead space may affect the results. In other words, differences in the slopes might be due to an error in measuring P_ICO_2. Specifically, there might be a difference between P_ICO_2 measured at the mouth and alveolar P_ICO_2 due to the effect of dead space when measuring HCVR. Because our subjects were in a semisitting position, this dead space effect might have been the result of the mechanism reported by Larson and Severinghaus[5].

Hazinski et al.[1] have also reported that in infants the slope is between 0.22 and 0.78. This wide range may be the result of using PCO_2 in both the X-axis as the stimulus and the Y-axis as the response. Another explanation is that as PCO_2 rises, the response is computed from the difference between numbers that are approaching each other, so any measurement errors increase when inspired CO_2 is high.

Another source of error with the Hazinski method is the assumption that CO_2 excretion remains constant, even when PCO_2 is increased. This is almost certainly incorrect to a small extent because body stores gradually increase at higher PCO_2 levels.

Despite these sources of error, our directly measured values were similar to values we obtained with the Hazinski method. The slope of the values obtained with the Hazinski method and the slope of the directly measured HCVR were strongly correlated.

We conclude that the Hazinski method is useful for estimating directly measured HCVR.

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