postulated to account for gas exchange, including Taylor dispersion and turbulence, asymmetric velocity profiles, pendelluft, cardiogenic mixing, collateral ventilation and molecular diffusion [6].

Helium is a noble gas, with very low atomic weight (4 g/mol) and density (0.157 g/L at 37°C and 1 atm). The density of helium-oxygen mixture reduces the resistance factor in gas delivery [7]. This increased mobility has three effects: gas more readily reaches the alveoli, thus allowing greater diffusion; breathing effort is significantly reduced by using a less-dense gas; and carbon dioxide is eliminated more rapidly through a helium-oxygen mixture than through a nitrogen-oxygen mixture [8-10]. In HFOV with helium, both properties may contribute to improved ventilation [11]. Winters et al. reported a case series of children with respiratory acidosis during HFOV. When the carrier gas was changed to a helium-oxygen mixture, CO_2 clearance improved [12]. Helium-oxygen mixtures have been examined using HFOV in animal models [9,10,13]. Those experiments showed that the improvement of ventilation with a helium-oxygen mixture was related to a larger Vt delivery by the oscillator under the same amplitude (AMP). If Vt during HFOV is maintained at a constant level, use of a helium-oxygen mixture does not alter gas exchange in HFOV ventilators with either a membrane-driven oscillator [10] or a piston-driven oscillator [13].

Continuous tracheal gas insufflation (TGI) is a technique that flushes dead space, and may thus allow reductions in respiratory support. Kakous et al. [14] reported the effects of continuous TGI in conventional ventilation. The effect of TGI is based mainly on the replacement of end-tidal gas in the instrumental dead space with an inspiratory gas mixture.

We hypothesized that a helium-oxygen mixture delivered into the trachea using a TGI technique (0.3 L/min) would enhance CO_2 elimination during HFOV. The purpose of this study was to compare the effects of TGI on gas exchange using helium-oxygen and nitrogen-oxygen mixtures in a rabbit model during HFOV.

Methods

Bench test

To elucidate the physical effects of reducing gas density during HFOV with TGI, we performed a bench test utilizing a test lung. A schematic of the experimental system is shown in Figure 1. The test lung (NeoLung; IngMar Medical, PA) was connected to the endotracheal tube (ETT) with a monitoring lumen (internal diameter, 3.5 mm; Mallinckrodt, St. Louis, MO), and attached to the circuit of a piston-driven high-frequency ventilator (Humming II; Metran, Saitama, Japan). Static compliance and resistance of the test lung were1.3 $mL/cmH_2O/kg$ and 160 $cmH_2O/L/s/kg$, respectively. Pressure at the Y-piece of the circuit was monitored using a pressure sensor (AP-C35; Keyence, Osaka, Japan). The carrier gas (nitrogen-oxygen or helium-oxygen mixture, 78:22 mixture ratio; bias flow rate, 8 L/min) inside the HFOV circuit was oscillated using the piston-driven Humming II with mean airway pressure set at 12 cmH_2O, stroke volume (SV) at 15 mL, and frequency at 15 Hz.

In the series of HFOV with TGI, the carrier gas inside the HFOV circuit was a nitrogen-oxygen mixture (78:22 mixture ratio). Insufflating gas flow (nitrogen-oxygen mixture, 78:22 mixture ratio; or helium-oxygen mixture, 78:22 mixture ratio) through

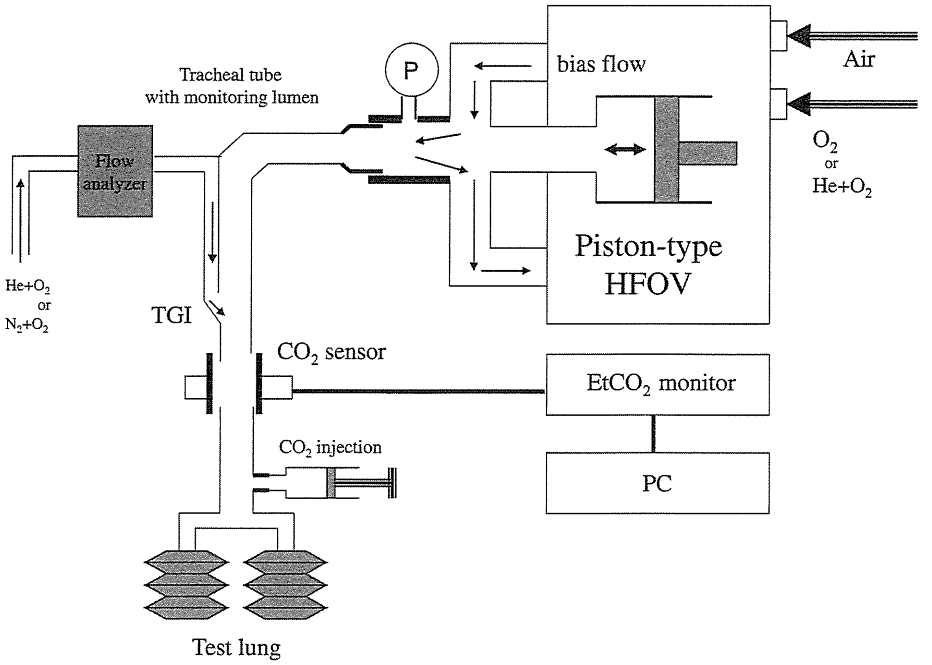

Figure 1 Schematic of the experimental system. The carrier gas (nitrogen-oxygen mixture or helium-oxygen mixture; bias flow rate, 8 L/min) inside the HFOV circuit was oscillated with mean airway pressure set at 12 cmH_2O, stroke volume at 15 mL, and frequency of 15 Hz. Helium-oxygen mixture was supplied at the O_2 port of the ventilator. In the series of HFOV with TGI, insufflating gas flow (nitrogen-oxygen mixture or helium-oxygen mixture) through the monitoring lumen of the ETT was 0.3 L/min.

the monitoring lumen of the ETT was 0.3 L/min. We used a helium-calibrated flow analyzer (PF-300; ImtMedical, Buchs, Switzerland) to ensure that TGI flow of the two gases was equal. To compare the speed of CO_2 transport, 5 ml of tracer gas (CO_2) was injected into the system through an access port near the test lung. CO_2 partial pressure at the end of the ETT was monitored using an $EtCO_2$ monitor (OLG-2800; Nihon Kohden, Tokyo, Japan). Real-time data from the $EtCO_2$ monitor were collected using a computerized data accumulation system at a sampling rate of 200 samples/s. The single exponential curve describing the CO_2 concentration inside the system for 3 s was approximated by nonlinear regression (Excel 2010; Microsoft, WA). We used the equation: measured CO_2 concentration = $a\ \exp^{-b\ t}$, where a and b are the variables obtained by curve fitting and t is the time of CO_2 measurement from the point at which CO_2 concentration was 100 mmHg, representing the upper limit of the measurement capability of the $EtCO_2$ monitor. All experiments were repeated six times.

Animal preparation

All study protocols were approved by the Institutional Animal Care and Use Committee of Shinshu University, Nagano, Japan. Three Japanese white rabbits (body weight, 2.309 ± 0.131 kg) were used in the study. Animals were premedicated by intramuscular administration of midazolam (10 mg/kg/dose) and xylazine (5 mg/kg/dose). The ear vein was cannulated using a 24-G angiocatheter for intravenous anesthesia and hydration. Animals were placed in a supine position under a radiant warmer to maintain body temperature throughout the entire study period, and body temperature was

Tmonitored using a rectal temperature probe. Tracheotomy was performed, and a no-cuff ETT with monitoring lumen (internal diameter, 3.5 mm; Mallinckrodt), was inserted to a depth of 3 cm from the lower edge of the cricoid cartilage and fixed in place. Intermittent ventilation (IMV) was initiated using a time-cycled, pressure-limited ventilator (Humming II; Metran). Using a digital pressure sensor (AP-C40; Keyence) installed into the Y-piece of the breathing circuit, actual pressure parameters were measured and registered.

Static compliance and resistance were measured by the passive expiratory flow-volume method, using a pneumotachograph (LFM-317 Aivision Laminar Flow Meter, Metabo, Lausanne, Switzerland). During this procedure, we confirmed that no leakage was present. Anesthesia and myoparalysis were provided by continuous intravenous infusion of midazolam (0.1 mg/kg/h), xylazine (3 mg/kg/h) and pancuronium (0.1 mg/kg/h). The carotid artery was then cannulated for direct blood pressure measurement, heart rate (HR) monitoring and determination of arterial blood gases (ABG).

Interventions and measurements

Animals were allowed 20 min for stabilization under IMV. After sustained inflation maneuver at 20 cmH_2O for 10 s, ventilation mode was shifted to the HFOV mode of the same ventilator (Humming II; Metran). ABG was obtained after 10 min of ventilation with: mean airway pressure (MAP), 12 cmH_2O; frequency, 15 Hz; FiO_2, 0.30; and bias flow rate, 8 L/min. SV (same as Vt) was adjusted to 4.16 ± 0.57 ml (mean ± standard deviation) to obtain permissive hypercapnia. The target $PaCO_2$ was 70 mmHg. Amplitude (AMP) was a subordinate factor during HFOV with the piston-driven oscillator, which was influenced by SV, animal airway condition (especially compliance) and the nature of the gas in the circuit. After baseline recordings were taken, tracheal gas was insufflated through the second monitoring lumen of the ETT for 10 min at gas flow of 0.3 L/min. In our preliminary experiment in healthy rabbits, steady state was reached after approximately 5 min during HFOV with TGI. After data collection with a nitrogen-oxygen mixture (70:30 mixture ratio), the gas for TGI was switched to a helium-oxygen mixture (70:30 mixture ratio, 0.487 g/L at 37°C and 1 atm) and

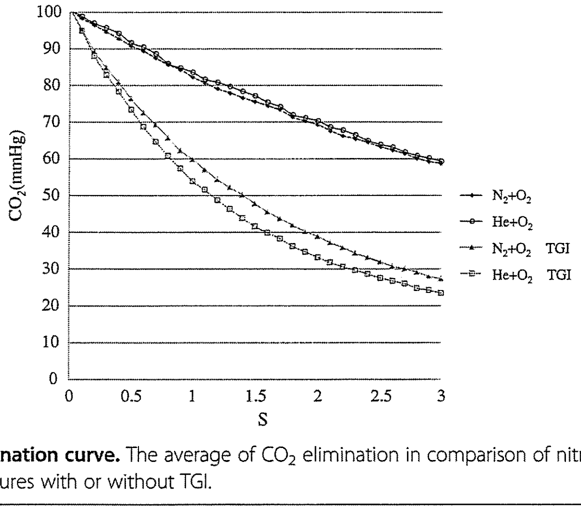

Figure 2 CO_2 elimination curve. The average of CO_2 elimination in comparison of nitrogen-oxygen and helium-oxygen mixtures with or without TGI.

Table 1 Effects of the speed of CO2 transport on the time constant

Insufflating gas	Non-linear regression	b	Time constant = 1/|b|
Helium-oxygen	$y = 91.641e^{-0.4848x}$	−0.4848	**2.06**
	$y = 91.24e^{-0.4986x}$	−0.4986	**2.01**
	$y = 89.045e^{-0.4748x}$	−0.4748	**2.11**
	$y = 91.327e^{-0.4936x}$	−0.4936	**2.03**
	$y = 93.579e^{-0.4859x}$	−0.4859	**2.06**
	$y = 92.799e^{-0.492x}$	−0.492	**2.03**
			mean ± SD 2.05 ± 0.04
Nitrogen-oxygen	$y = 94.984e^{-0.436x}$	−0.436	**2.29**
	$y = 94.806e^{-0.436x}$	−0.436	**2.29**
	$y = 94.334e^{-0.436x}$	−0.436	**2.29**
	$y = 95.175e^{-0.4367x}$	−0.4367	**2.29**
	$y = 93.381e^{-0.4321x}$	−0.4321	**2.31**
	$y = 96.175e^{-0.437x}$	−0.437	**2.29**
			mean ± SD 2.3 ± 0.01
Bias flow gas	**Non-linear regression**	**b**	**Time constant = 1/|b|**
Helium-oxygen	$y = 101.18e^{-0.182x}$	−0.182	**5.49**
	$y = 100.9e^{-0.181x}$	−0.181	**5.52**
	$y = 99.006e^{-0.1774x}$	−0.1774	**5.64**
	$y = 100.35e^{-0.1807x}$	−0.1807	**5.53**
	$y = 101.64e^{-0.1797x}$	−0.1797	**5.56**
	$y = 99.601e^{-0.1771x}$	−0.1771	**5.65**
			mean ± SD 5.57 ± 0.06
Nitrogen-oxygen	$y = 99.37e^{-0.1925x}$	−0.1925	**5.19**
	$y = 98.925e^{-0.1801x}$	−0.1801	**5.55**
	$y = 100.75e^{-0.1751x}$	−0.1751	**5.71**
	$y = 99.517e^{-0.1738x}$	−0.1738	**5.75**
	$y = 100.72e^{-0.1733x}$	−0.1733	**5.77**
	$y = 96.836e^{-0.1912x}$	−0.1912	**5.23**
			mean ± SD 5.54 ± 0.26

ventilated for 10 min before obtaining data. After data collection with the helium-oxygen mixture (70:30), the gas for TGI was returned to the nitrogen-oxygen mixture (70:30), and allowed 10 min to stabilize before data collection. HFOV settings were held constant while the gas mixture of TGI was changed. The cycle of changing the gas mixture from nitrogen-oxygen mixture to helium-oxygen mixture and back was performed three times per animal. To ensure that animal conditions returned to baseline after each experiment, rabbits were ventilated under HFOV without TGA.

Statistics

Data were analyzed by Wilcoxon *t*-test, one-way analysis of variance (ANOVA) or repeated-measures ANOVA, followed by the Bonferroni test to compare matched experimental sets. All data are presented as mean ± standard error of the mean. Significance was defined for values of $p < 0.01$.

Results

Bench test

The CO_2 elimination curve is shown in Figure 2. Speed of CO_2 transport is expressed as the time for the CO_2 concentration to reach 63% of the final concentration (time constant). Effects of the speed of CO_2 transport on the time constant are summarized in Table 1. When the carrier gas inside the HFOV circuit was changed without TGI, the time constant was 5.54 ± 0.26 s with the nitrogen-oxygen mixture and 5.57 ± 0.06 s with the helium-oxygen mixture. When the gas for TGI was changed to a low-density gas, speed of CO_2 transport increased, as reflected by a significant fall in time constant from 2.3 ± 0.01 s with the nitrogen-oxygen mixture to 2.05 ± 0.04 s with the helium-oxygen mixture ($p < 0.01$).

Animal experiments

We compared $PaCO_2$ and PaO_2 values obtained after 10 min of TGI with each of the two gas mixtures (Figure 3). Compared with the nitrogen-oxygen mixture, the helium-oxygen mixture reduced $PaCO_2$ by 7.6 mmHg ($p < 0.01$) and improved PaO_2 by 14 mmHg ($p < 0.01$). AMP during TGI was significantly lower with the helium-oxygen mixture than with the nitrogen-oxygen mixture ($p < 0.01$) and did not significantly impact MAP (Table 2).

Discussion

Helium may alter gas exchange during HFOV via a number of mechanisms. Because helium is less dense than nitrogen, the frictional forces in turbulent flows are reduced with helium as compared to oxygen-enriched air. For a given set of airway dimensions, turbulent flow results in a higher resistance than laminar flow. In addition, mechanical ventilation through a narrow ETT and airway, particularly in pediatric and neonatal patients, may further increase the Reynolds number, thus resulting in greater turbulent flow [15,16]. With helium, the calculated Reynolds number is lower (<200), which may change regions of turbulent flow to laminar flow, reducing resistance and energy leakage. As resistive forces and

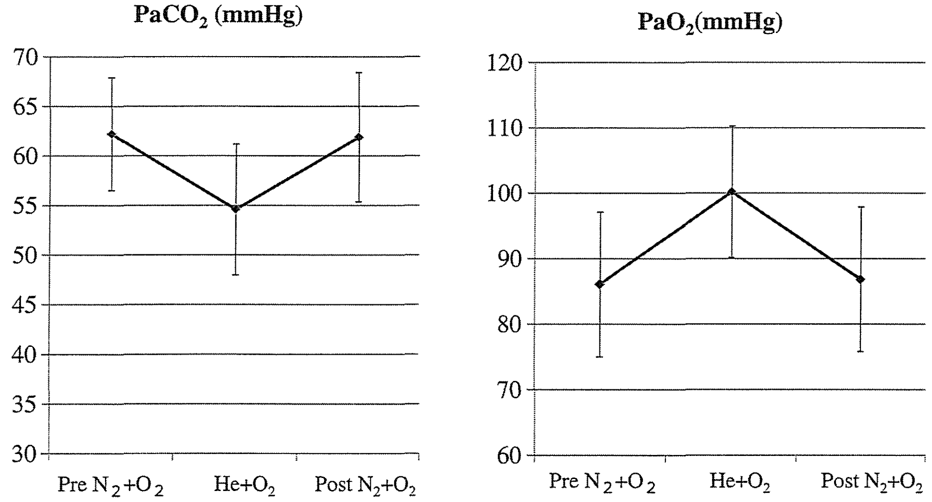

Figure 3 $PaCO_2$ and PaO_2 under TGI. The gas mixture under TGI was changed from nitrogen-oxygen to helium-oxygen and back.

Table 2 AMP and MAP change during the animal experiment

	No TGI	TGI $N_2 + O_2$	TGI $He + O_2$	TGI $N_2 + O_2$	TGI $He + O_2$	TGI $N_2 + O_2$	TGI $He + O_2$	TGI $N_2 + O_2$	No TGI
Rabbit 1 AMP (cm H_2O)	19	19.2	17.4*	19.5	17.7*	19.3	17.2*	19.2	19.8
Rabbit 2 AMP (cm H_2O)	17.5	17.5	15.9*	17.5	16.1*	17.9	16*	17.6	17.8
Rabbit 3 AMP (cm H_2O)	15.8	15.9	14.2*	16	14.4*	16	14.4*	16.1	16.3
Rabbit I MAP (cm H_2O)	12	11.9	11.7	12	11.6	11.8	11.6	11.8	12
Rabbit 2 MAP (cm H_2O)	12	12	12.1	12.2	12.1	12.2	12	12.1	12.1
Rabbit 3 MAP (cm H_2O)	12.7	12.7	12.7	12.9	12.7	12.9	12.8	12.7	12.8

AMP amplitude, *MAP* mean air-way pressure, *TGI* tracheal gas insufflation.
*: $p < 0.01$.

energy dissipation are decreased, tidal volume per oscillation increases. This theory has been confirmed before in a laboratory study [8]. In theory, because of its lower density, helium may favorably alter gas exchange through the pendelluft effect, inhalation/exhalation flow asymmetry, Taylor dispersion, and molecular diffusion [9].

By flushing dead space, continuous TGI may allow reductions in respiratory support. The effect of continuous TGI is based mainly on the replacement of end-tidal gas in the instrumental dead space with an inspiratory gas mixture. Continuous TGI allows the use of low-volume ventilation over a prolonged period and reduces the duration of mechanical ventilation in preterm infants [17]. To facilitate CO_2 transport without increasing SV and AMP, a helium-oxygen mixture was administered to the turbulent zone using TGI techniques.

When using a helium-oxygen mixture for TGI, CO_2 excretion speed increases under constant SV. This effect is attributed to the nature of helium in the turbulent zone. A significant decrease in $PaCO_2$ was shown in animal experiments performed to reproduce the effects apparent in the bench test. The concentration of helium in the test lung that resulted from mixing the TGI flow with the main flow was same as main flow. When we supplied 0.6 ml/min of TGI flow, helium-oxygen was not needed on the ventilator. We therefore propose that TGI offers a very simple, cost-effective means of supplying helium-oxygen during HFOV, without the need to adapt/calibrate the ventilator for the use with helium-oxygen and avoiding the high gas consumption associated with a high bias flow rate.

One limitation of the present study was that our experiment was performed in normal animal lungs. The low density of helium does not always reduce resistance [18]. Different types and phenotypes of obstructive airway disease manifest in different regions of the lung. The effectiveness of TGI on helium-oxygen mixture HFOV may thus differ according to the type of obstructive airway disease. Further research using lung injury models is therefore warranted.

Conclusion

This study demonstrated that a helium-oxygen mixture delivered into the trachea using a tracheal gas insufflation (TGI) technique enhances CO_2 elimination and offers a simple cost-effective means of achieving helium-oxygen mixture HFOV.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AB participated in the design of the study and performed the statistical analysis. TN conceived of the study, participated in its design and coordination and helped to draft the manuscript. TA participated in the design of the study and performed the statistical analysis. KK participated in the design of the study and performed the statistical analysis. All authors have read and approved the final manuscript.

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A lightweight mainstream capnometer with very low dead space volume is useful monitor for neonates with spontanous and mechanical ventilation: Pilot study*

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ABSTRACT

Objects: The purpose of this study was to observe a correlation between $P_{ET}CO_2$ and $PaCO_2$ in intubated neonates under intermittent mandatory ventilation with spontaneous breathing. Material and methods: A total of 55 paired $P_{ET}CO_2$ measured by mainstream capnometry and $PaCO_2$ values were obtained from 4 intubated neonates in our neonatal intensive care units at Nagano Children's Hospital, Nagano, Japan. Results: $P_{ET}CO_2$ and $PaCO_2$ were significantly correlated ($r^2 = 0.928$, $p < 0.0001$). For samples in ventilated neonates with spontaneous breathing, maximum $P_{ET}CO_2$ and mean $P_{ET}CO_2$ correlated strongly with $PaCO_2$ (maximum $P_{ET}CO_2$: $r^2 = 0.9401$, $p < 0.0001$; mean $P_{ET}CO_2$: $r^2 = 0.8587$, $p < 0.0001$). Although $PaCO_2$ also correlated with minimum $P_{ET}CO_2$ ($r^2 = 0.2884$, $p < 0.01$) in ventilated infants with spontaneous breathing, a significant difference was seen with maximum $P_{ET}CO_2$ ($p < 0.05$) and mean $P_{ET}CO_2$ ($p < 0.05$) in the correlation coefficient r between $PaCO_2$ and $P_{ET}CO_2$. Conclusion: Present study showed that a good correlation exists between $P_{ET}CO_2$ and $PaCO_2$ in intubated neonates under intermittent mandatory ventilation with spontaneous breathing. Lightweight with low amounts of dead space mainstream capnometry can be used as noninvasive monitor in incubated neonates with spontaneous breathing.

Keywords: Capnography; Neonate

1. INTRODUCTION

Capnography, which displays the level and waveform of CO_2 in exhaled air, is a simple technique that appears to accurately indicate arterial PCO_2 ($PaCO_2$) and provides information on cell metabolism, blood perfusion, and alveolar ventilation [1-3]. The use of end-tidal CO_2 ($P_{ET}CO_2$) for monitoring and as a tool for verifying endotracheal tube (ETT) position is another common practice in the operating room and in adult and pediatric intensive care units [3]. This procedure was also introduced to neonatal intensive care units (NICUs), but there are limitations of the technique in smaller babies, especially for extremely low birth weight infants due to issues such as the weight of sensors or water droplets within circuits, dead space, and leakage from tracheal intubation tubes. Recently, a lightweight mainstream capnometer was developed. We have previously reported a strong correlation between $P_{ET}CO_2$ and $PaCO_2$ under controlled ventilation when tidal volume/body weight (TV/BW) was 6 - 15 mL/kg and the leakage rate was <60% in rabbits. Furthermore, under conditions of 6 mL/kg of tidal volume (TV), $PaCO_2$ was significantly increased by a dead space increase of only 1 mL, representing >7% of TV [4].

Capnometry is expected as one of the non-invasive monitor in NICUs. Although several investigators have demonstrated good relationships between values for $P_{ET}CO_2$ and $PaCO_2$ in infants [5-8], the value of capnometry in estimating $PaCO_2$ has been questioned during anesthesia with spontaneous ventilation [9,10]. On the other hand, while TV is larger than spontaneous breaths, $P_{ET}CO_2$ is close to the $PaCO_2$ and to that observed with voluntary maximal expiration [11]. The purpose of this study was to observe a correlation between $P_{ET}CO_2$ and $PaCO_2$ in intubated neonates under intermittent mandatory ventilation (IMV) with spontaneous breathing.

2. MATERIAL AND METHODS

A total of 55 paired $P_{ET}CO_2$ and $PaCO_2$ values were obtained from the 4 neonates who had been admitted to the NICU at Nagano Children's Hospital between April and July 2009. Neonates deemed as non-viable by the attending physician were excluded, as were those with

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*Competing interests: The authors have no competing interests to declare.

conditions such as acute shock, infection, or hemodynamic instability. Before enrollment into this study, informed consent was obtained from the parents or guardian of each infant. Study subjects comprised 4 neonates. Mean (±standard deviation (SD)) gestational age and birth weight were 36.7 ± 2.1 weeks and 2446 ± 487 g, respectively. Data on demographics, clinical characteristics, and laboratory findings for subjects were collected by referring to the clinical laboratory records.

The infants were ventilated mechanically using a time-cycled pressure-limited ventilator (Calliope®; Metran, Saitama, Japan). Peak inspiratory pressure (PIP), fraction of inhaled oxygen (FiO_2), inspiratory time, positive end expiratory pressure (PEEP) and respiratory rate were settled to provide the optimal arterial PaO_2 and $PaCO_2$ as defined by the neonatologists and were not manipulated for the purposes of the study.

Mainstream $P_{ET}CO_2$ was measured via a capnograph connected to the proximal end of the endotracheal tube (Cap-One®; TG-970P, Nihon-Kohden, Tokyo, Japan). Data was continuously recorded on a laptop computer using the software programmed by LabVIEW (National Instruments, Texas, USA) through CO_2 monitor (OLG-2800; Nihon-Kohden, Tokyo, Japan) each patients. We distinguished between spontaneous breaths and ventilator breaths on the basis of capnography for 20 s at the time of blood gas analysis. For each 20-s sample period, we determined the maximum, mean and minimum values of $P_{ET}CO_2$ (**Figure 1**). Measurements of $P_{ET}CO_2$ that did not show an alveolar plateau due to a large amount of leakage were excluded.

The tidal volume was measured by mainstream capnography (CO2SMO 8100, Fukuda Denshi, Tokyo, Japan). The leakage ratio was calculated using the following equation:

$$\text{Leakage ratio} = \frac{(\text{Inspiratory TV} - \text{Expiratory TV})}{\text{Inspiratory TV}} \times 100$$

Blood samples were drawn from indwelling arterial lines into a 0.1-mL heparinized syringe to prevent coagulation. Blood sampling was performed by heel puncture when arterial line was not placed. Measurements were then immediately made using a bedside blood gas analyzer (ABL 700; Radiometer, Copenhagen, Denmark) for $PaCO_2$. Blood gas analysis was performed for the purposes of evaluation of the patient (including PaO_2, $PaCO_2$, electrolytes or lactate, etc.) only. Calibrations were performed automatically for the blood gas analyzer and the accuracy of the capnography was checked by 5% CO_2 gas cylinder.

All statistical analyses were conducted using SPSS Statistics version 17.0 (SPSS, Chicago, Illinois). To determine whether $P_{ET}CO_2$ were representative of $PaCO_2$, the relationship between $P_{ET}CO_2$ and $PaCO_2$ was analyzed by simple linear regression. The standard technique of Fisher's Z transformation was performed to determine whether a significant difference existed in the correlation coefficient r between $PaCO_2$ and each group of $P_{ET}CO_2$.

Furthermore, Bland-Altman plots were performed to assess measurements of $P_{ET}CO_2$. Bland-Altman plots demonstrate "good agreement" not only when differences between methods are consistent across all measurements but also when the differences are small. In a situation in which the difference between measurements is expected to change based on a third variable, Bland-Altman plots lose importance. Precision of $P_{ET}CO_2$ and the agreement between $P_{ET}CO_2$ and $PaCO_2$ were assessed by bias, SD and calculating the 95% confidence interval (CI) for the bias (bias = $P_{ET}CO_2 - PaCO_2$). Values of $p < 0.05$ were determined to be significant.

This study was carried out under the control of the Ethics Committee of Medicine and Medical Care, Nagano Children's Hospital, Nagano, Japan.

3. RESULTS

Mean TV/BW and leakage ratio were 7.3 ± 1.7 mL/kg and 9.5% ± 12.0%, respectively (**Table 1**). All patients were treated using sedative drugs.

$P_{ET}CO_2$ and $PaCO_2$ were significantly correlated ($r^2 = 0.928$, $p < 0.0001$). In the Bland-Altman plot test, the mean difference (bias) and SD of the differences for

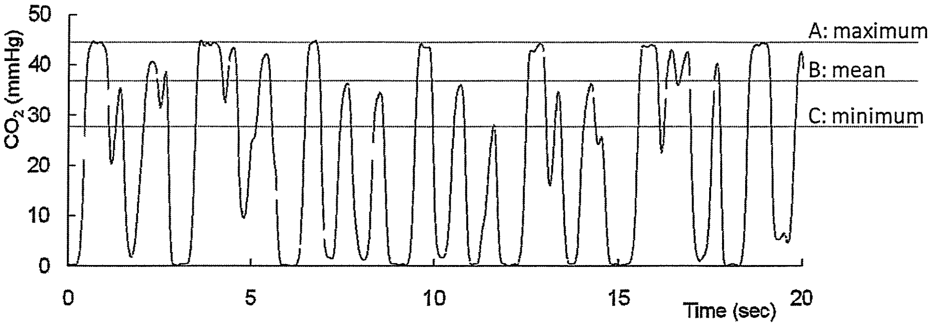


Figure 1. Continuous recording of $P_{ET}CO_2$. For each 20-s sample period, we determined maximum A, mean B and minimum C $P_{ET}CO_2$.

Table 1. Baseline characteristics.

Characteristics	Number of patients
Sex	
Male	3
Female	1
Inborn/Outborn	
Inborn	3
Outborn	1
Underlying disease	
Congenital heart disease	2
Intraventricular hemorrhage	1
Perioperative management	1
Gestational age (week)	
Mean ± SD	36.7 ± 2.1
Range	34 – 39
Birthweight (g)	
Mean ± SD	2446 ± 487
Range	1778 - 2894
Tidal volume/Body weight (mL/kg)	
Mean ± SD	7.3 ± 1.7
Range	4.8 - 8.6
Leakage ratio (%)	
Mean ± SD	9.5 ± 12.0
Range	0 - 27

$P_{ET}CO_2$ was −0.88 ± 2.69 mmHg (95% CI for the bias, −1.61 to −0.16 mmHg) (**Figure 2**). We chose the maximum for $P_{ET}CO_2$ on the basis of capnograms for each 20-s period at the time of blood gas analysis.

Due to breath-to-breath variation, we evaluated three measurements of $P_{ET}CO_2$ to determine which one most consistently and accurately predicted $PaCO_2$. From 55 measurements, we have selected 24 paired $P_{ET}CO_2$ and $PaCO_2$ values which were obtained at the time when spontaneous breathing was present.

For samples in ventilated infants with spontaneous breathing, maximum $P_{ET}CO_2$ and mean $P_{ET}CO_2$ correlated strongly with $PaCO_2$ (maximum $P_{ET}CO_2$: $r^2 = 0.9401$, $p < 0.0001$; mean $P_{ET}CO_2$: $r^2 = 0.8587$, $p < 0.0001$). Although $PaCO_2$ also correlated with minimum $P_{ET}CO_2$ ($r^2 = 0.2884$, $p < 0.01$) in ventilated infants with spontaneous breathing, a significant difference was seen with maximum $P_{ET}CO_2$ ($p < 0.05$) and mean $P_{ET}CO_2$ ($p < 0.05$) in the correlation coefficient r between $PaCO_2$ and $P_{ET}CO_2$ (**Figures 3(a)-(c)**).

Bland-Altman analysis showed that $P_{ET}CO_2$ underestimated $PaCO_2$ by a mean difference (bias) of −0.175 ± 2.31 mmHg (95% CI for the bias, −1.15 to 0.799 mmHg) in the maximum $P_{ET}CO_2$, −5.01 ± 3.55 mmHg (95% CI for the bias, −6.50 to −3.51 mmHg) in mean $P_{ET}CO_2$, and −14.6 ± 8.82 mmHg (95%CI for the bias, −18.3 to −10.9 mmHg) in minimum $P_{ET}CO_2$ (**Figures 3(d)-(f)**).

4. DISCUSSION

Advances in the treatment of neonatal respiratory failure, including exogenous surfactant [12,13], inhaled nitric oxide (iNO) [14,15], and a growing repertoire of assisted ventilation strategies [16] have decreased morbidity and mortality rates. Patient monitoring has played a critical role in the safe and effective application of these advanced therapies.

Pulse oximetry provides a noninvasive method of assessing oxygenation and continuous surveillance of the partial pressure of arterial oxygen [17]. Maintaining $PaCO_2$ within the desired range by frequent arterial sampling can increase the need for multiple transfusions in the NICU [18], highlighting the need for methods of continuous non-invasive monitoring of CO_2 levels. Both hypocarbia and hypercarbia are detrimental to extremely low birth weight infants and have been implicated as

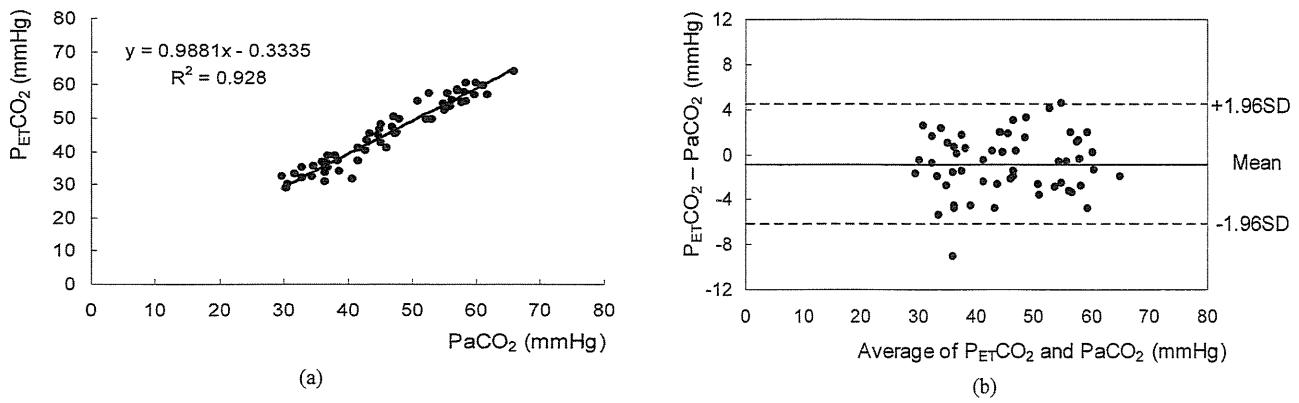
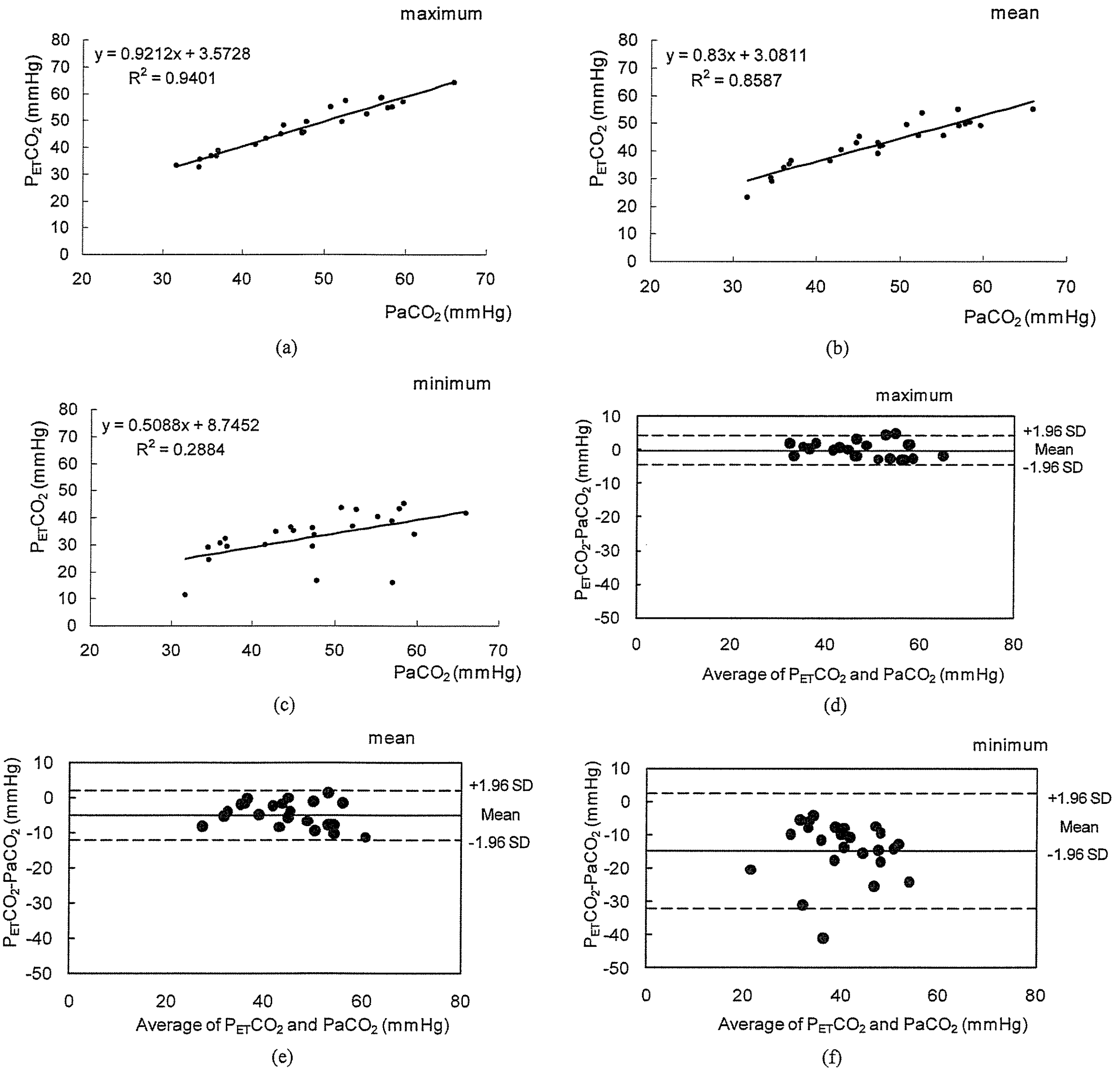


Figure 2. The relationship between $P_{ET}CO_2$ and $PaCO_2$ (a) and Bland-Altman plot shows bias against average values of $P_{ET}CO_2$ and $PaCO_2$ in ventilated infants (b). $P_{ET}CO_2$ and $PaCO_2$ were significantly correlated ($r^2 = 0.928$, $p < 0.0001$).



(a) (b) (c) (d) (e) (f)

Figure 3. The relationship between $P_{ET}CO_2$ and $PaCO_2$ (a), (b) and (c) and Bland-Altman plot shows bias against average values of $P_{ET}CO_2$ and $PaCO_2$ in ventilated infants with spontaneous breathing (d), (e) and (f). Maximum $P_{ET}CO_2$ and mean $P_{ET}CO_2$ correlated strongly with $PaCO_2$. Conversely, $PaCO_2$ did not correlate with minimum $P_{ET}CO_2$.

causative factors in periventricular leukomalacia, intraventricular hemorrhage and chronic lung disease [19-21]. Critical event analyses have documented that hypoxemia secondary to depressed respiratory activity is a principal risk factor for near misses and death [22,23].

Monitoring of $P_{ET}CO_2$ is a simple and noninvasive technique that appears to accurately indicate $PaCO_2$ in a variety of clinical situations [1,24]. However, levels of $P_{ET}CO_2$ and $PaCO_2$ depend on ventilation, cardiac output, CO_2 output, and pulmonary function; a change in any of these will cause a change in $P_{ET}CO_2$ [25]. For instance, a growing degree of difference between $P_{ET}CO_2$ and $PaCO_2$ can indicate the severity of pulmonary embolism [26] or even the effects of thrombolytic therapy [27].

$P_{ET}CO_2$ varied appreciably from breath to breath. The reliability of this value under conditions of significant ventilation perfusion inequality or heterogeneous tidal volumes has thus been questioned [28]. In many cases, spontaneous breaths of variable tidal volumes far outnumbered ventilator breaths, but still contributed relatively little to alveolar minute ventilation. We found that maximum $P_{ET}CO_2$ during each sampling period showed the best correlation with $PaCO_2$. A number of investigators have suggested that larger tidal volumes are necessary to measure $P_{ET}CO_2$ accurately, as small (e.g., spontaneous) breaths may fail to "wash out" the anatomic dead space [11,29].

Weinger *et al.* [30] also found a wide range in differences between $P_{ET}CO_2$ and $PaCO_2$ over time. However, they measured mean peak $P_{ET}CO_2$ over a period of 8 min. Although averaging maximal $P_{ET}CO_2$ values over a longer time span might improve the stability and reliability of $PaCO_2$ - $P_{ET}CO_2$, assessing the respiratory status to measure $P_{ET}CO_2$ over a long time would be difficult. The respiratory apparatus might change second to second.

Takano *et al.* [31] reported that reliable $P_{ET}CO_2$ was obtained when a vital capacity maneuver was performed on each nonintubeted patient, indicating that full expiration to the maximal expiratory position is necessary for precise estimation of $PaCO_2$.

Comparison with spontaneous breathing, end tidal CO_2 measured from ventilated breath is close to the $PaCO_2$ and to that observed with a voluntary maximal expiration. This PCO_2 gradient between ventilator and spontaneous breathing indicates a large dead-space to tidal volume ratio; much of the expired CO_2 appearing with spontaneous breathing is diluted, with dead space air lowering the concentration at any point during expiration.

Although our prospective observational study revealed a good correlation and agreement between $PaCO_2$ and maximum $P_{ET}CO_2$, the present study included only a very small number of participants, and the conditions of patients were not constant. Furthermore, in children with congenital cyanotic heart disease, right-to-left intracardiac shunting reportedly causes an obligatory difference between $PaCO_2$ and $P_{ET}CO_2$ [32,33]. Our subjects included patients with congenital heart disease because they showed stable cardiorespiratory status in this study.

This study consisted of only a small number of participants, the statistical implications of repeated measurements in the same infants, and the conditions of the cases were not constant. In addition, we did not adjust for cardiac output their measurements, though differences in cardiac output are known to affect $P_{ET}CO_2$ measurements [25]. Therefore, we would like to study these issues in the future.

5. CONCLUSION

Our results indicate that a good correlation exists between $P_{ET}CO_2$ and $PaCO_2$ in intubated neonates under intermittent mandatory ventilation with spontaneous breathing. Furthermore, maximum $P_{ET}CO_2$ correlated strongly with $PaCO_2$ compared to minimum $P_{ET}CO_2$. Lightweight with low amounts of dead space mainstream capnometry can be used as noninvasive monitor in incubated neonates with spontaneous breathing.

6. ACKNOWLEDGEMENTS

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Research and Reports in Neonatology

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METHODOLOGY

$P_{ET}CO_2$ measured by a new lightweight mainstream capnometer with very low dead space volume offers accurate and reliable noninvasive estimation of $PaCO_2$

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Objective: Although capnometers are widely used in adult and pediatric intensive care units, they are not widely used in neonatal intensive care units due to issues such as the weight of sensors, dead space, and leakage from tracheal intubation tubes. These authors developed a light and low dead space airway adaptor of end-tidal carbon dioxide pressure ($P_{ET}CO_2$) and evaluated the correlations between $P_{ET}CO_2$ and partial CO_2 pressure ($PaCO_2$) in rabbits while changing tidal volume and leakage volume.

Methods: Firstly, Japanese rabbits weighing 2 kg were divided into three tidal volumes (6 mL/kg, 10 mL/kg, or 15 mL/kg), and $P_{ET}CO_2$ and $PaCO_2$ were measured. Secondly, the respiratory apparatus was set to a tidal volume/body weight ratio of 10 mL/kg, leakage rates were divided into seven groups, and $P_{ET}CO_2$ and $PaCO_2$ were measured.

Results: $P_{ET}CO_2$ and $PaCO_2$ were significantly correlated ($r^2 = 0.9099$, $P < 0.0001$) when there was no leakage in the tracheal intubation tubes. No significant differences were observed between $PaCO_2$ and $P_{ET}CO_2$ ($P_{a\text{-}ET}CO_2$) in the three tidal volume/body weight groups or for groups in which leakage rate was <60%, but significant deviations in $P_{a\text{-}ET}CO_2$ were noted in groups with leakage rate 60%.

Conclusion: There was a strong correlation between $P_{ET}CO_2$ and $PaCO_2$ when tidal volume/body weight ratio was 6–15 mL/kg with leakage rate <60%. Lightweight mainstream capnometer with a low amount of dead space airway adaptor might be useful in very low birth weight infants with small tidal volume.

Keywords: capnography, mainstream, neonate

Introduction

Advancements in the treatment of neonatal respiratory failure, including exogenous surfactant,[1,2] inhaled nitric oxide,[3,4] and a growing repertoire of assisted ventilation strategies,[5] have decreased morbidity and mortality rates. Patient monitoring has played a critical role in the safe and effective application of these advanced therapies.

Maintaining partial carbon dioxide pressure ($PaCO_2$) within the desired range by frequent arterial sampling can increase the need for multiple transfusions in the neonatal intensive care unit,[6] so methods for continuous noninvasive monitoring of CO_2 levels would prove extremely useful. Both hypocarbia and hypercarbia are detrimental to extremely low birth weight infants and have been implicated as causative factors in periventricular leukomalacia, intraventricular hemorrhage, and chronic lung disease.[7–9] Critical event analyses have documented hypoxemia secondary to depressed

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respiratory activity as a principal risk factor for near misses and death.[10,11]

Capnography, which displays the level and waveform of CO_2 in exhaled air, provides information on cell metabolism, blood perfusion, and alveolar ventilation[12] with noninvasive indirect methods. Use of end-tidal CO_2 pressure ($P_{ET}CO_2$) for monitoring and as a tool for verifying endotracheal tube position is a common practice in the operating room and in adult and pediatric intensive care units.[12] However, so far capnometers are not used widely in neonates due to issues such as the weight of sensors and water droplets within circuits, dead space, and leakage from tracheal intubation tubes.

These authors developed a new light (6 g) and low dead space (1 mL) airway adapter (YG-213T; Nihon-Kohden Corporation, Tokyo, Japan) for mainstream capnography (Cap-ONE TG-970P; Nihon-Kohden). The objective of this study was to evaluate the correlations between $P_{ET}CO_2$ and $PaCO_2$ in rabbits while changing tidal volume (TV) and leakage volume with this device.

Material and methods

Ten adult Japanese rabbits weighing 2 kg were anesthetized by intramuscular injection of ketamine at 10 mg/kg and xylazine at 5 mg/kg, and a 24 G catheter (JELCO, Smiths Medical Italia Srl, Mirano, Italy) was placed in the ear vein for continuous intravenous infusion of anesthetic agents. Rabbits were placed in a supine position throughout the experiment. After tracheotomy, an endotracheal tube (internal diameter, 2.5 mm; Mallinkrodt, Inc, St Louis, MO) was inserted. A 24 G catheter was placed in the internal carotid artery to allow collection of samples for blood gas analysis and to monitor arterial blood pressure and heart rate using biomedical research system (LEG-1000; Nihon-Kohden). Anesthesia was provided by continuous intravenous infusion of ketamine (5 mg/kg/hour) and paralysis was maintained by continuous administration of pancuronium (0.1 mg/kg/hour). Animals were administered a mixture of 0.45% sterile saline and 10% glucose solution at 3 mL/kg/hour during the experiment. Body temperature was continuously monitored and maintained at 38.5°C–39.5°C using a heating pad.

Rabbits were ventilated mechanically with a time-cycled pressure-limited ventilator (Humming II; Metran Co, Ltd, Saitama, Japan) adjusted to: fraction of inhaled oxygen at 0.6; inspiratory time at 0.6 seconds; and positive end-expiratory pressure at 5 cmH_2O. Peak inspiratory pressure was settled at the TV maintained at TV/body weight (BW) ratios of 6 mL/kg, 7 mL/kg, 10 mL/kg, and 15 mL/kg, as measured by pneumotachography (ARFEL-VR; Aivision Corporation, Tokyo, Japan). Respiratory rate was adjusted to a level at which normocapnia was maintained (41.6 ± 3.8 mmHg). In the investigation of the effects on TV/BW, TV/BW was divided into three groups (6 mL/kg, 10 mL/kg, and 15 mL/kg), and $P_{ET}CO_2$ and $PaCO_2$ was measured.

$P_{ET}CO_2$ was monitored in intubated rabbits by mainstream capnography (Cap-One TG-970P; Nihon-Kohden). Mainstream $P_{ET}CO_2$ was measured via a capnograph connected to the proximal end of the endotracheal tube. Before each blood sampling, an adequate reading of $P_{ET}CO_2$ and a reliable waveform on the mainstream capnograph (continuous steady waveform of expired CO_2 throughout the ventilatory cycle) was taken. Data was continuously recorded on a laptop computer using the software programmed by LabVIEW (National Instruments Corporation, Austin, TX) for each rabbit. $PaCO_2$ was measured from samples withdrawn intermittently from intraarterial lines indwelling in the internal carotid artery (ABL700; Radiometer Medical ApS, Bronshoj, Denmark). The amount of leakage was adjusted by fixation of the tracheal intubation tubes. The leakage ratio was calculated using the following equation:

$$\text{Leakage ratio} = (\text{inspiratory TV} - \text{expiratory TV}) / \text{inspiratory TV } 100 \times 100$$

The end-tidal volume was measured by mainstream capnography (CO2SMO 8100, Fukuda Denshi, Tokyo, Japan) and also leakage rate was calculated with CO2SMO 8100. The respiratory apparatus was set to a TV/BW ratio of 10 mL/kg, then leakage rates were divided into seven groups (0%–10%, 10%–30%, 30%–50%, 50%–60%, 60%–70%, 70%–80%, and 80%–100%), and $P_{ET}CO_2$ and $PaCO_2$ were measured.

$PaCO_2$ was measured with the additional dead space caused by attachment of a CO_2 sensor and additional dead space in the setting of TV/BW ratios of 6 mL/kg, 7 mL/kg, and 10 mL/kg.

Statistical analyses were conducted using SPSS Statistics version 17.0 software (SPSS, Inc, Chicago, IL). To determine whether $P_{ET}CO_2$ values were representative of $PaCO_2$, the relationship between $P_{ET}CO_2$ and $PaCO_2$ was analyzed by simple linear regression. Bland–Altman plots, representing a visual assessment of agreement between two methods of measurement, were created to assess the measurement of $P_{ET}CO_2$. Bland–Altman plots demonstrate "good agreement" not only when differences between methods are consistent across all measurements but also when the differences are small. In a situation in which difference between the two measurements is expected to change based on a third variable, Bland–Altman plots lose importance. The precision of $P_{ET}CO_2$ measurements and agreement between $P_{ET}CO_2$ and $PaCO_2$ values were assessed by bias ($PaCO_2 - P_{ET}CO_2$), standard deviation, and 95% confidence interval (CI) for the bias. One-factor analysis of variance and the Mann–Whitney U test were used to compare differences between subgroups of TV/BW and leakage ratio. Values of $P < 0.05$ were considered significant. The present study was conducted with the approval of the Institutional Animal Care and Use Committee of Nagano Children's Hospital, Nagano, Japan.

Results

A total of 43 measurements of $P_{ET}CO_2$ and $PaCO_2$ were analyzed. Under conditions of no leakages in the tracheal intubation tubes, $P_{ET}CO_2$ and $PaCO_2$ were significantly correlated ($r^2 = 0.9099$, $P < 0.0001$; Figure 1) and the Bland–Altman plot test showed a mean difference (bias) for $P_{ET}CO_2$ of −0.876 mmHg (Figure 2). The 95% CI for this bias was −1.80–0.04 mmHg. The 95% CI of limits of agreement was −6.74–4.99 mmHg.

In the comparison of differences between $PaCO_2$ and $P_{ET}CO_2$, when setting the TV/BW to 6 mL/kg, 10 mL/kg or 15 mL/kg, no significant differences were observed between the three groups (Figure 3).

Figure 4 shows the effects of additional dead space on $PaCO_2$ under TV conditions of 12 mL, 14 mL, or 20 mL. Under TV conditions of 12 mL and 14 mL (6 mL/kg and 7 mL/kg, respectively), $PaCO_2$ was significantly increased by a dead space increase of only 1 mL, but under TV conditions of 20 mL (10 mL/kg), a dead space increase of 1 mL did not significantly increase $PaCO_2$. $PaCO_2$ thus seemed to be increased by dead space increases representing 7% of TV.

Figure 5 shows the effects of leakage rate on $PaCO_2/P_{ET}CO_2$ at a TV/BW of 10 mL/kg. For all leakage rates <60%, no significant differences were seen between $PaCO_2$ and $P_{ET}CO_2$ compared to the group with a leakage rate of 0%–10%. However, groups with leakage rate 60% showed significant deviations between $PaCO_2$ and $P_{ET}CO_2$.

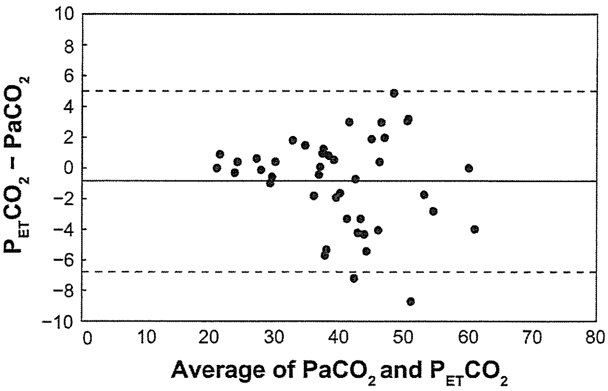

Figure 2 In the Bland–Altman plot test, the mean difference (bias) and standard deviation of differences for end-tidal carbon dioxide pressure ($P_{ET}CO_2$) was −0.876 ± 2.99 mmHg. The 95% confidence interval for bias was −6.74 to 4.99 mmHg.
Abbreviation: $PaCO_2$, partial CO_2 pressure.

Regarding the expiratory plateau phase, a relatively constant PCO_2 was maintained when alveolar mixed gas was expired, as shown by the capnogram for 10 mL/kg TV/BW and leakage ratio <60% (Figure 6).

Discussion

It was found that $P_{ET}CO_2$ measured by mainstream capnography cap-ONE was an accurate and reliable noninvasive method for estimating $PaCO_2$, showing a good correlation with $PaCO_2$ ($r^2 = 0.9099$, $P < 0.0001$), and there is no bias in the measurement (95% CI: −1.80–0.04 mmHg).

$P_{ET}CO_2$ can be feasibly measured by mainstream or sidestream capnography. Measuring $P_{ET}CO_2$ reportedly underestimates alveolar CO_2 due to the relatively low TVs and rapid respiratory rates of newborns.[13,14] The CO_2 waveform (capnogram) has been characterized for adult patients with normal and abnormal pulmonary function.[15,16] In newborns,

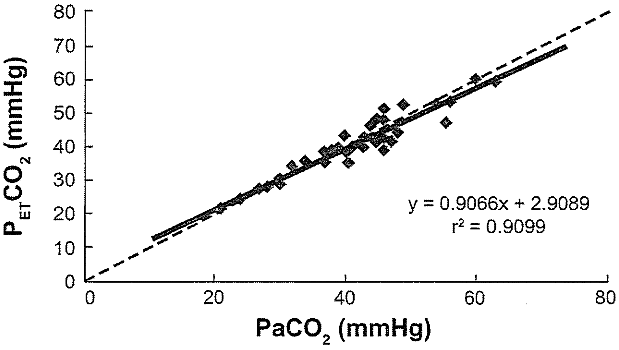

Figure 1 End-tidal carbon dioxide pressure ($P_{ET}CO_2$) and partial CO_2 pressure ($PaCO_2$) were significantly correlated ($r^2 = 0.9099$, $P < 0.0001$).
Note: Dotted line is the line of identity.

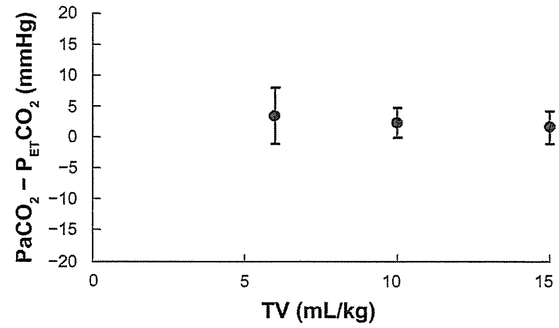

Figure 3 In the comparison of differences between end-tidal carbon dioxide pressure ($P_{ET}CO_2$) and partial CO_2 pressure ($PaCO_2$), no significant differences were observed between the three groups with tidal volume (TV)/body weight ratio of 6 mL/kg, 10 mL/kg, and 15 mL/kg.

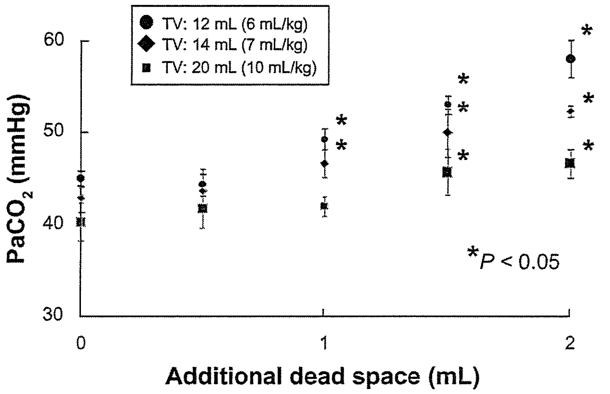

Figure 4 Effects of additional dead space on partial carbon dioxide pressure ($PaCO_2$) under conditions of 12 mL or 20 mL of tidal volume (TV). Under conditions of 12 mL of TV (6 mL/kg), $PaCO_2$ was significantly increased by a dead space increase of only 1 mL. Under conditions of 20 mL of TV (10 mL/kg), even a dead space increase of 1 mL did not significantly increase $PaCO_2$. $PaCO_2$ appears to be affected by a dead space increase of >7% of TV.

CO_2 waveform slurring (a spurious decrease in the slope of the ascending phase of the capnogram) occurs due to dilution of exhaled gas when small, rapid breath packets are measured in a relatively large sample cell.[17]

Condensed water and patient secretions may also impede both mainstream and sidestream technologies. Furthermore, relative inaccuracy is seen in conditions of ventilation-perfusion mismatch.[18,19]

Transcutaneous CO_2 monitoring is a noninvasive technique for measuring CO_2 levels. However, transcutaneous CO_2 monitoring is not tolerated in very low birth weight infants because of their fragile skin, and the technique is affected by acidosis and hypoxia.[20,21]

Mainstream capnography has been found to be more accurate,[22–24] but the sensor position used for mainstream capnography is connected inline between the proximal endotracheal tube and ventilator circuit. As a result, dead space is increased, the sensor competes for TV, and sensor weight may kink the endotracheal tube. When a flow sensor is connected to the endotracheal tube, use of mainstream capnography is even more cumbersome.[25] Given these limitations, most neonatal intensive care units do not routinely perform capnography to assess and manage ventilatory status. These problems might be reduced in measurement of $P_{ET}CO_2$ if the sensor is lightweight and the dead space is small.

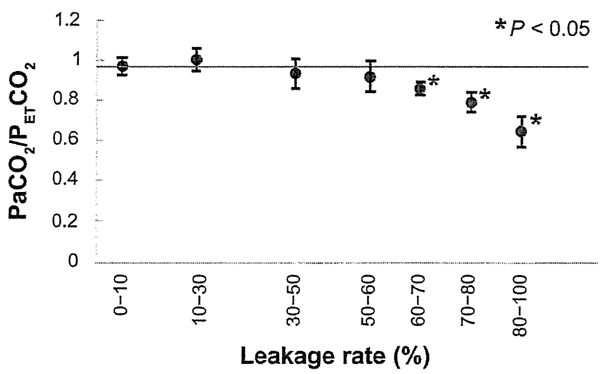

Figure 5 Effects of leakage rate on end-tidal carbon dioxide pressure ($P_{ET}CO_2$) and partial CO_2 pressure ($PaCO_2$). When leakage rate was <60%, no significant differences were seen between $PaCO_2$ and $P_{ET}CO_2$ compared to the group in which the leakage rate was 0%–10%. However, groups with leakage rate 60% showed significant deviations between $PaCO_2$ and $P_{ET}CO_2$.

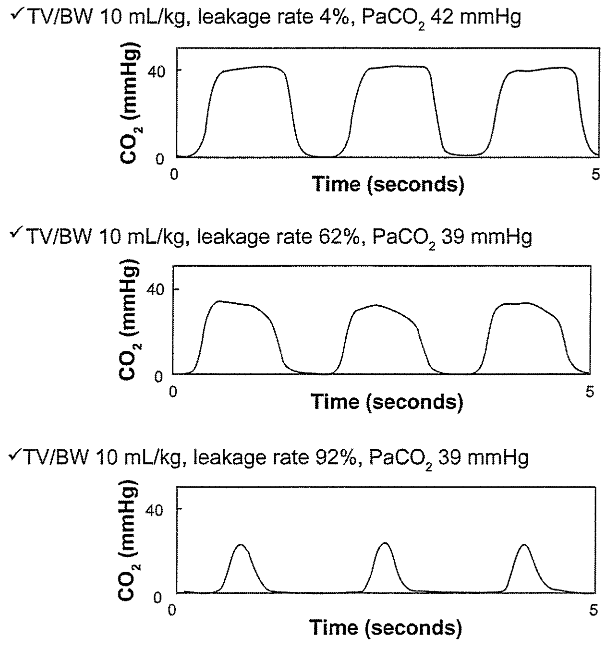

Figure 6 Regarding the expiratory plateau phase, when alveolar mixed gas was expired, a relatively constant partial CO_2 pressure ($PaCO_2$) was maintained, as shown by the capnogram for the >6 mL/kg tidal volume/body weight (TV/BW) group.

In the comparison of differences between $PaCO_2$ and $P_{ET}CO_2$, when setting the TV/BW to 6 mL/kg, 10 mL/kg, or 15 mL/kg, no significant differences were observed between the three groups even at the 6 mL/kg setting. Conversely, Sakamoto et al reported a lower correlation between $PaCO_2$ and $P_{ET}CO_2$ with ≤6 mL/kg compared to >6 mL/kg in porcine neonates.[26] They measured $P_{ET}CO_2$ by sidestream capnography, so $P_{ET}CO_2$ might have been underestimated.

Figure 4 shows the effects of additional dead space on $PaCO_2$. Under conditions of 6 mL/kg of TV, $PaCO_2$ was significantly increased by a dead space increase of only 1 mL, representing >7% of TV. Figueras et al[27] reported that the introduction of the pneumotachometer, which has a dead space of 1.6 mL for 10 minutes, led to a transcutaneous PCO_2 increase of 5.40 ± 2.66 mmHg, from 39.76 ± 8.69 mmHg to 45.17 ± 9.22 mmHg ($P = 0.0000$) in newborn infants. However, they did not measure $PaCO_2$ directly, nor they did change the amount of dead space when measuring transcutaneous PCO_2.

With respect to lung injury, too high volumes/pressures and/or too low positive end expiratory pressure promotes degradation of the lungs, so-called ventilator-induced lung injury, and is associated with high mortality.[28] Such injuries are known to result in local alterations in lung compliance and pulmonary edema secondary to capillary leakage and are important contributing factors to the pathogenesis of chronic lung disease in neonates.[29,30]

To the best of the authors' knowledge, no studies have described the effects of endotracheal tube leakage on $P_{ET}CO_2$. Leakage is more of a problem in children than in adults because of the use of uncuffed endotracheal tubes. Capnography offers direct monitoring of the inhaled and exhaled concentrations or partial pressure of CO_2. The amount of endotracheal tube leakage around an uncuffed endotracheal tube is thus larger, and significant differences between $PaCO_2$ and $P_{ET}CO_2$ might arise.

No significant differences were found between $PaCO_2$ and $P_{ET}CO_2$ when the leakage rate was $<60\%$, similar to the group in which leakage rate was 0%–10%. However, in groups with a leakage rate 60%, significant deviations were seen between $PaCO_2$ and $P_{ET}CO_2$.

Also, regarding the expiratory plateau phase, a relatively constant PCO_2 was maintained, as shown by the capnogram for 10 mL/kg TV/BW and leakage ratio $<60\%$ (Figure 6).

This analysis of rabbits weighing 2 kg revealed good correlation and agreement between $PaCO_2$ and $P_{ET}CO_2$. However, only deep anesthetized rabbits weighing 2 kg were used. In addition, $P_{ET}CO_2$ was measured in rabbits using the setting of limited mechanical ventilation. Further studies using different conditions are warranted to further elucidate this area.

Conclusion

A strong correlation was obtained and there was no bias between $P_{ET}CO_2$ and $PaCO_2$ when TV/BW was 6–15 mL/kg and the leakage rate was $<60\%$. Lightweight and low amounts of dead space capnometer may be used in very low birth weight infants with small TV.

Disclosure

The authors report no conflicts of interest in this work.

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