Accuracy of a battery-powered portable capnometer in premature infants

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Abstract
Carbon dioxide measurement is useful for confirmation of successful tracheal intubation and ensuring adequate ventilation. There are two types of CO2 detectors, i.e., single-use-only colorimetric devices and capnometers. Although portable capnometers are widely used for resuscitation, there have been no reports regarding their clinical utility in neonates. The correspondence between end-tidal CO2 (PetCO2) level determined using a battery-powered portable capnometer and arterial CO2 (PaCO2) was investigated using paired data obtained simultaneously from 26 neonates weighing 1262 ± 589 g at examination on mechanical ventilation. PetCO2 level and PaCO2 showed a strong correlation (r = 0.839, P < 0.001), and the correlation equation was: PetCO2 = 0.8 × PaCO2 + 1.1. Therefore, PetCO2 readings obtained with a battery-powered portable capnometer were likely to be underestimated. This became more pronounced with decreasing infant body weight at examination as the net difference in measurements of PaCO2 and PetCO2 was significantly positively correlated with infant body weight at examination (r = 0.451, P < 0.001). The observations presented here may be helpful in the use of battery-powered portable capnometers in neonates requiring controlled ventilation with tracheal intubation.

Keywords End-tidal CO2 · Capnometer · Premature infants

1 Introduction
Measurement of carbon dioxide (CO2) using a CO2 detector is a useful method for confirming airway clearance [1]. However, colorimetric devices are qualitative rather than quantitative. It is important to control CO2 in premature infants, especially during the acute phase, such as resuscitation, during transportation from the delivery room to the neonatal intensive care unit (NICU). However, during transportation after birth or resuscitation, ventilation is manually supported. Considering that cerebral blood flow (CBF) correlates directly with PaCO2, continuous management of ventilation based on the monitoring of CO2 is capable of limiting fluctuation in PaCO2 and CBF [2]. It is important to visually and continuously confirm the end-tidal CO2 using a capnometer, which also helps the respiratory therapist to determine the appropriate initial settings when switching to a ventilator from a manual support. The capnometer, which measures CO2 expired from the lung alveoli as PetCO2 and generally installed in anesthesia machines, is used to identify early airway incidents and to ensure adequate ventilation in the operating room, out of hospital, and during transport of critically ill patients [3–5]. However, conventional capnometer devices are challenging to monitor CO2 correctly due to the dead volume at the sensor in neonates, especially in premature infants. Neonatal resuscitation is usually conducted in the delivery room or operation room, after which the infant is transported to NICU. Therefore, there is a need for a portable capnometer that can be used easily and monitor correctly at resuscitation or during transportation in emergency, delivery, and operation rooms. The EMMA™ capnograph (EMMA, Masimo, Danderyd, Sweden) is small, light (5.2 × 3.9 × 3.9 cm and 59.5 g with batteries), is readily portable, does not require routine calibration before use, can be warmed up in a short time, 1 ml of the dead volume as small as possible, and can be used for continuous monitoring of CO2 [6].

Respiratory function includes oxygenation of blood and expiration of CO2. Premature neonates often have difficulties
in respiration and require tracheal intubation immediately after birth for controlled ventilation. SpO2 monitoring is recommended during resuscitation and transportation of neonates with respiratory failure to the NICU [7]. However, SpO2 monitoring alone without CO2 monitoring is insufficient as SpO2 is only an indicator of binding O2 to hemoglobin. SpO2 monitor provides no information about CO2 levels and is not useful to estimate respiratory acidosis caused by hypercapnia due to inadequate respiration. In neonates, it is important to control CO2 levels to prevent both hyper and hypocapnia although permissive hypercapnia may be used to protect the lungs, hypercapnia and subsequent respiratory acidosis, which occurs after birth, may exacerbate pulmonary hypertension and make it persistent [8]. On the other hand, hypocapnia is related to brain injury [9]. Hyperventilation with subsequent hypocapnia was widely practiced strategy in the past [10]. In the 1980s, hyperventilation was the only method available for the treatment of persistent pulmonary hypertension (PPHN). Inhalation of nitric oxide (NO) and extracorporeal membrane oxygenation (ECMO) were not commonly accepted as treatment options. However, artificially initiated hypocapnia by hyperventilation is now recognized as a major risk factor for intracranial intraventricular hemorrhage (IVH) or periventricular leukomalacia (PVL) [11]. Hypocapnia causes brain vasoconstriction, and thus reduces cerebral blood flow (CBF) [10]. The brain vasculature at watershed areas is particularly underdeveloped and vulnerable to hypoperfusion in premature infants at around 32 weeks of gestation, and PVL can occur in this area. IVH is caused by multiple reasons, one of which is hypocapnia [10–12]. Severe IVH is related to neurodevelopmental delay, and 48% of cases of IVH are observed within the first 6 h of life. Therefore, strict control of blood CO2 levels in the acute phase is required [12, 13].

To our knowledge, there have been no studies focusing on the accuracy of the EMMA capnograph in neonates. This study was performed to assess the accuracy of the EMMA capnograph in neonates on mechanical ventilation by comparing end-tidal CO2 measured using this device with PaCO2.

2 Materials and methods

This study was approval by the institutional review board (IRB) of Kagoshima City Hospital (KCH) (20150903). Neonates admitted to the NICU of KCH between July 2014 and February 2015 and requiring controlled ventilation were eligible for inclusion in the study. The parents of all patients provided written informed consent before participation in this study. Two mainstream capnographs are used for patients on mechanical ventilation in KCH, EMMA and CapONE™ (Nihon Kohden, Tokyo). Sidestream capnography is not used. The EMMA was placed distal to the endotracheal tube using a neonatal adaptor with 1.0-mL dead space. PaCO2 levels were measured using 100-μL arterial blood sample, and PetCO2 levels were recorded at the same time as sampling as a number without a decimal point. Each participant underwent PetCO2 measurement at least once a day. Participants on mechanical ventilation required repeated PetCO2 measurements during their hospital stay when arterial blood samples were collected. PaCO2 was measured using an ABL 800™ (Radiometer, Copenhagen, Denmark). All measurements were recorded with the patient in the supine position. Blood gas analysis was performed when ordered by the attending neonatologist depending on the condition of the patient.

Statistical analyses were performed using the JMP13© statistical software package (SAS, Cary, NC). The Wilcoxon/Kruskal–Wallis method was used for analysis of continuous variables. Fisher’s exact probability test was used for analysis of categorical variables. Regression analysis was performed. In all analyses, \( P < 0.05 \) was considered statistically significant.

3 Results

The study population consisted of 26 newborn infants (Table 1). The median (minimum–maximum) gestational age at birth was 27 (22–38) weeks and median birth weight was

| Table 1 Demographic characteristics of the 26 patients |
|---------------------------------------------|
| Male/female | 12 (46%)/14 (54%) |
| Gestational week at birth | 27 (22–38) |
| 22–26 | 12 (46%) |
| 27–32 | 9 (35%) |
| 33– | 5 (19%) |
| Birth weight (g) | 881 (420–2730) |
| <999 | 15 (58%) |
| 1000–1499 | 3 (11%) |
| 1500–2499 | 7 (27%) |
| ≥2500 | 1(4%) |
| EMMA application | 63 |
| Total no. of applications | 3 (1–5) |
| Once | 8 (13%) |
| Twice | 5 (16%) |
| Three times | 9 (42%) |
| Four times | 2 (13%) |
| Five or more | 2 (16%) |
| Corrected age (weeks) | 30 (22–38) |
| Body weight (g) | 1151 (420–2730) |
| Tidal volume (mL/kg) | 5.6 (3.3–7.4) |
881 (420–2730) g. Tracheal tubes were selected according to birth weight as follows: < 1000 g, Fr. 2.5; 1000–1800 g, Fr. 3.0; and > 1800 g, Fr. 3.5. At the point of measurement, the ventilation mode was synchronized intermittent mechanical ventilation (SIMV) without volume guarantee and the leak-age displayed on the ventilator was 0% in all patients. Simul-
taneous EMMA PetCO2 and PaCO2 measurements were
performed 63 times in the 26 infants (median, three times
per infant). Median values of corrected age, body weight,
and tidal volume of those measured with EMMA were 30
(22–38) weeks of gestation, 1151 (420–2730) g, and 5.6
(3.3–7.4) mL/kg, respectively (Table 1). No adverse events
associated with use of the EMMA capnograph occurred in
the 26 infants.

3.1 Correlation between PetCO2 and PaCO2

As shown in Fig. 1, the majority of PetCO2 measurements
were lower than those of PaCO2. However, the correlation
coefficient (r) was 0.839 and the correlation equation was as
follows for 63 paired data: PetCO2 = 0.80 × PaCO2 + 1.17.
Thus, the overall PetCO2 measurements were approximately
20% lower than PaCO2 measurements.

3.2 Effects of infant body weight on PetCO2 measurements

The body weights of the infants showed no significant cor-
relation with PaCO2 measurements, but were significantly
positively correlated with PetCO2 measurements (Fig. 2,
upper and middle panels). As most PetCO2 measurements
were lower than those of PaCO2 (Fig. 1), these results sug-
gested that PetCO2 measurements were more likely to be
underestimated in infants with lower body weight. This was
the case, as shown in the lower panel of Fig. 2, where net
differences between measurements of PaCO2 and PetCO2
increased as infant body weight decreased. However, the
net differences were not significantly correlated with tidal
volume (mL/kg) at the time of examination.

4 Discussion

In this study, PetCO2 measured using an EMMA capno-
graph in neonates was correlated with PaCO2. This is the
first report of the application of this device to neonates,
including extremely infants with low birth weight. As shown
in Fig. 1, correlations between PetCO2 and PaCO2 were
observed over wide ranges; PaCO2 [24.5–84.5] and PetCO2
[18–79]. These observations also showed that the EMMA
capnograph correctly tracked PaCO2 over a wide range with
PetCO2 approximately 20% lower than PaCO2. The reason
of this gap, especially in premature infants, was reported as
ventilatory parameters, small airways, missing alveolar pla-
tee, airway dead spaces, endotracheal tube leaks, apparatus
deep space, response time and sampling rate [14]. Singh
et al. have reported lower levels of PetCO2 relative to PCO2,
not PaCO2, in side stream device, meaning PetCO2 is lower
than PaCO2 [15]. Several neonatal lung diseases affecting
gas exchange subsequent to cause the gap between PCO2
and PetCO2 were also reported, and the effects of lung stiff-
ness related with surfactant activity have a relation with the
gap [16]. No infants with the diseases were included in the
present study. Our data showed that the net difference of
detected CO2 was larger in infants with lower birth weight.
As lower CO2 values were observed in lower birth weight
infants, higher dead space relative to tidal volume were considered. PetCO₂ was measured with a sensor set at the distal end of the tracheal tube, which was also the end of the entire ventilation circuit. In management of mechanical ventilation, tidal volume per weight (TV mL/kg) is a score that ensures that the ventilator settings are adequate for the patient. The normal range of TV mL/kg in neonates is 4–6 mL/kg. Obviously, the net tidal volume (mL) is smaller in infants with lower birth weight. In this study, the median body weight and median TV mL/kg at the time of examination were 1151 (420–2730) g and 5.6 (3.3–7.4) mL/kg, respectively. TV mL/kg was adequate for each body weight. Low net tidal volume has been reported as a factor of the observed net differences between PaCO₂ and PetCO₂ due to the lack of alveolar plateau [17]. Our result indicates that a greater net tidal volume was required for accuracy of PetCO₂ measurement in premature infants. Therefore, net tidal volume affects PetCO₂ depending on the level of flow at the sensor. The differences also have been due to differences in the sizes of tracheal tubes. Use of a tracheal tube of inadequate size affect tidal volume, because the tracheal tubes used in neonates do not have a cuff, therefore tidal volume is affected by air leakage. In this study, air leakage displayed on the ventilator monitors was 0% at each examination.

5 Conclusion

The results of this study indicated that PetCO₂ measured using an EMMA capnograph was positively correlated to PaCO₂ even in preterm neonates. Thus, this device may be applicable even in preterm neonates. As shown in the correlation equation, PetCO₂ determined with the EMMA capnograph was approximately 20% lower than PaCO₂. Therefore, this underestimation must be taken into account when assessing blood CO₂ level using this device.

Author contributions E.H., and S.I. contributed to the study design and writing the manuscript. All authors have seen and approved the final version of this manuscript.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Ethical Approval The Institutional Review Board of the Kagoshima city hospital approved the protocol of the current studies (20150903).

Informed consent Written informed consent was obtained from each participant or authorized representative prior to study enrollment.
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